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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Sep 29  The Philippines Inventory of Chemicals and Chemical
                  Substances (PICCS) has been added to CHEMLIST
 NEWS  3  Oct 27  New Extraction Code PAX now available in Derwent
                  Files
 NEWS  4  Oct 27  SET ABBREVIATIONS and SET PLURALS extended in
                  Derwent World Patents Index files
 NEWS  5  Oct 27  Patent Assignee Code Dictionary now available
                  in Derwent Patent Files
 NEWS  6  Oct 27  Plasdoc Key Serials Dictionary and Echoing added to
                  Derwent Subscriber Files WPIDS and WPIX
 NEWS  7  Nov 29  Derwent announces further increase in updates for DWPI
 NEWS  8  Dec  5  French Multi-Disciplinary Database PASCAL Now on STN
 NEWS  9  Dec  5  Trademarks on STN - New DEMAS and EUMAS Files
 NEWS 10  Dec 15  2001 STN Pricing
 NEWS 11  Dec 17  Merged CEABA-VTB for chemical engineering and
                  biotechnology
 NEWS 12  Dec 17  Corrosion Abstracts on STN
 NEWS 13  Dec 17  SYNTHLINE from Prous Science now available on STN
 NEWS 14  Dec 17  The CA Lexicon available in the CAPLUS and CA files
 NEWS 15  Jan 05  AIDSLINE is being removed from STN
 NEWS 16  Feb 06  Engineering Information Encompass files have new names
 NEWS 17  Feb 16  TOXLINE no longer being updated

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 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
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FILE 'HOME' ENTERED AT 10:44:33 ON 18 APR 2001

=> file medline caplus embase biosis
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.15       0.15

FILE 'MEDLINE' ENTERED AT 10:44:42 ON 18 APR 2001

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=> s MJ? and TCR and (RTPCR or PCR)
L1            0 MJ? AND TCR AND (RTPCR OR PCR)

=> s MJ? and aplpha
L2            0 MJ? AND APLPHA

=> MJ? and TCR
MJ? IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s MJ? and TCR
L3            6 MJ? AND TCR

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4            3 DUP REM L3 (3 DUPLICATES REMOVED)

=> dis l4 1-3 ibib abs kwic

L4   ANSWER 1 OF 3  MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:   1998313352      MEDLINE
DOCUMENT NUMBER:    98313352
TITLE:              Energy of adhesion of human T cells to adsorption layers of
                    monoclonal antibodies measured by a film trapping
                    technique.
AUTHOR:             Ivanov I B; Hadjiiski A; Denkov N D; Gurkov T D;
                    Kralchevsky P A; Koyasu S
CORPORATE SOURCE:   Laboratory of Thermodynamics and Physico-chemical
                    Hydrodynamics, Faculty of Chemistry, University of Sofia,
                    1126 Sofia, Bulgaria.
SOURCE:             BIOPHYSICAL JOURNAL, (1998 Jul) 75 (1) 545-56.
                    Journal code: A5S. ISSN: 0006-3495.
PUB. COUNTRY:       United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
```

WO 98 07870 1998 02 26

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY WEEK: 19981003

AB A novel method for studying the interaction of biological cells with interfaces (e.g., adsorption monolayers of antibodies) is developed. The method is called the film trapping technique because the cell is trapped within an aqueous film of equilibrium thickness smaller than the cell diameter. A liquid film of uneven thickness is formed around the trapped cell. When observed in reflected monochromatic light, this film exhibits an interference pattern of concentric bright and dark fringes. From the radii of the fringes one can restore the shape of interfaces and the cell. Furthermore, one can calculate the adhesive energy between the cell membrane and the aqueous film surface (which is covered by a layer of adsorbed proteins and/or specific ligands), as well as the disjoining pressure, representing the force of interaction per unit area of the latter film. The method is applied to two human T cell lines: Jurkat and its T cell receptor negative (**TCR**-) derivative. The interaction of these cells with monolayers of three different monoclonal antibodies adsorbed at a water-air interface is studied. The results show that the adhesive energy is considerable (above 0.5 **mJ**/m2) when the adsorption monolayer contains antibodies acting as specific ligands for the receptors expressed on the cell surface. In contrast, the adhesive energy is close to zero in the absence of such a specific ligand-receptor interaction. In principle, the method can be applied to the study of the interaction of a variety of biological cells (B cells, natural killer cells, red blood cells, etc.) with adsorption monolayers of various biologically active molecules. In particular, film trapping provides a tool for the gentle micromanipulation of cells and for monitoring of processes (say the activation of a T lymphocyte) occurring at the single-cell level.

AB . . . the latter film. The method is applied to two human T cell lines: Jurkat and its T cell receptor negative (**TCR**-) derivative. The interaction of these cells with monolayers of three different monoclonal antibodies adsorbed at a water-air interface is studied. The results show that the adhesive energy is considerable (above 0.5 **mJ**/m2) when the adsorption monolayer contains antibodies acting as specific ligands for the receptors expressed on the cell surface. In contrast,. . .

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:588743 CAPLUS
DOCUMENT NUMBER: 125:212708
TITLE: Receptor fusion proteins and chimeric genes encoding them and their use in the control of proliferation in the treatment of disease
INVENTOR(S): Capon, Daniel J.; Tian, Huan; Smith, Douglas H.; Winslow, Genine A.; Siekevitz, Miriam
PATENT ASSIGNEE(S): Cell Genesys, Inc., USA
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9623881	A1	19960808	WO 1996-US1292	19960202
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AZ, BY, KG, KZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5741899	A	19980421	US 1995-481003	19950607
US 5837544	A	19981117	US 1995-485293	19950607
US 6077947	A	20000620	US 1995-485598	19950607
CA 2221634	AA	19960808	CA 1996-2221634	19960202
AU 9648612	A1	19960821	AU 1996-48612	19960202
AU 715363	B2	20000203		
EP 821730	A1	19980204	EP 1996-904532	19960202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				

PRIORITY APPLN. INFO.: US 1995-382846 19950202
WO 1996-US1292 19960202

AB Chimeric receptors for proliferation-stimulating effectors are described for use in the treatment of disease (cancer, infectious, or autoimmune disease). The receptors are made up of combinations of domains from known receptors. One group has an extracellular clustering domain (ECD), transmembrane domain (TM), proliferation signaling domain (PSD) that can signal a host cell to divide. A second group has an intracellular clustering domain (ICD) and a proliferation signaling domain (PSD) that can signal a host cell to divide. A third group has an extracellular clustering domain (ECD) or an intracellular clustering domain (ICD), a transmembrane domain (TM), proliferation signaling domain (PSD), and an effector signaling domain that can signal an effector function and a host cell to divide. Chimeric genes for these receptors and methods for their expression and the therapeutic uses of the receptors and genes are described. The prepn. of fusion proteins of the ligand receptor and extracellular clustering domains of CD4 and Janus kinase or cytokine receptor subunits are described.

IT Plasmid and Episome
(pIKCD4-FKBP-**mJAK1**, chimeric gene for FK506-binding protein fusion with CD4 antigen and JAK1 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-FKBP-**mJAK2**, chimeric gene for FK506-binding protein fusion with CD4 antigen and JAK2 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-FKBP-**mJAK3**, chimeric gene for FK506-binding protein fusion with CD4 antigen and JAK3 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-Syk-**mJAK1**, chimeric gene for CD4 antigen .zeta. subunit fusion product with Syk and JAK1 kinases on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-Syk-**mJAK2**, chimeric gene for CD4 antigen .zeta. subunit fusion product with Syk and JAK2 kinases on; receptor fusion

proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-Syk-**mJAK3**, chimeric gene for CD4 antigen .zeta. subunit fusion product with Syk and JAK3 kinases on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-**mJAK1**, chimeric gene for CD4 antigen fusion product with JAK1 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-**mJAK2**, chimeric gene for CD4 antigen fusion product with JAK2 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-**mJAK3**, chimeric gene for CD4 antigen fusion product with JAK3 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-.zeta.-**mJAK1**, chimeric gene for CD4 antigen .zeta. subunit fusion product with JAK1 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-.zeta.-**mJAK2**, chimeric gene for CD4 antigen .zeta. subunit fusion product with JAK2 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKCD4-.zeta.-**mJAK3**, chimeric gene for CD4 antigen .zeta. subunit fusion product with JAK3 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKFKBP-**mJAK1**, chimeric gene for FK506-binding protein fusion with JAK1 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKFKBP-**mJAK2**, chimeric gene for FK506-binding protein fusion with JAK2 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKFKBP-**mJAK3**, chimeric gene for FK506-binding protein fusion with JAK3 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKSAb-FKBP-**mJAK1**, chimeric gene for sol. antibody fusion with FK506-binding protein and JAK1 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKSAb-FKBP-**mJAK2**, chimeric gene for sol. antibody fusion with FK506-binding protein and JAK2 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKSAb-FKBP-**mJAK3**, chimeric gene for sol. antibody fusion with FK506-binding protein and JAK3 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKSab-Syk-**mJAK1**, chimeric gene for sol. antibody fusion product with Syk and JAK1 kinases on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKSab-Syk-**mJAK2**, chimeric gene for sol. antibody fusion product with Syk and JAK2 kinases on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKSab-Syk-**mJAK3**, chimeric gene for sol. antibody fusion product with Syk and JAK3 kinases on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKSab-**mJAK1**, chimeric gene for sol. antibody fusion product with JAK1 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKSab-**mJAK2**, chimeric gene for sol. antibody fusion product with JAK2 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKSab-**mJAK3**, chimeric gene for sol. antibody fusion product with JAK3 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKSab-.zeta.-**mJAK1**, chimeric gene for sol. antibody-CD4 antigen .zeta. subunit fusion product with JAK1 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKSab-.zeta.-**mJAK2**, chimeric gene for sol. antibody-CD4 antigen .zeta. subunit fusion product with JAK2 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Plasmid and Episome
(pIKSab-.zeta.-**mJAK3**, chimeric gene for sol. antibody-CD4 antigen .zeta. subunit fusion product with JAK3 kinase on; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

IT Antigen receptors

Receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TCR (T-cell antigen receptor), fusion products; receptor fusion proteins and chimeric genes encoding them and their use in control of proliferation in treatment of disease)

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:542927 CAPLUS
DOCUMENT NUMBER: 113:142927
TITLE: Electron transport properties of thermodynamically stable aluminum-copper-ruthenium icosahedral quasicrystals
AUTHOR(S): Mizutani, U.; Sakabe, Y.; Shibuya, T.; Kishi, K.; Kimura, K.; Takeuchi, S.
CORPORATE SOURCE: Dep. Cryst. Mater. Sci., Nagoya Univ., Nagoya, 464-01, Japan
SOURCE: J. Phys.: Condens. Matter (1990), 2(28), 6169-78
CODEN: JCOMEL
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The electron transport properties of the thermodynamically stable Al68Cu17Ru15 quasicrystal were studied through the measurements of the electronic sp. heat coeff. and the temp. dependence of the elec. resistivity at 4.2-300 K. The full-width at the half max. for the strongest x-ray diffraction line (100000) is reduced to <0.15 nm-1 either by remelting the ingot with subsequent furnace cooling or by annealing the melt-spun ribbon at 850.degree. for 24 h. An apparent improvement in quasi-crystallinity upon the heat-treatment caused a drastic increase in resistivity up to 1600 .mu..OMEGA. cm and accompanied a very small electronic sp. heat coeff. .gamma. lower then 0.3 mJ mol-1 K-2. The temp. dependence of the resistivity characterized by a concave curvature with a neg. TCR can be discussed in terms of the weak localization of conduction electrons. The thermodynamically stable quasicrystals, like the present Al-Cu-Ru and the previously studied Al-Li-Cu, always exhibit a very low .gamma. value coupled with a high resistivity. The electron d. of states in thermodynamically stable quasicrystal may possess a structure-induced min., and the Fermi level does fall in this crit. range. An increase in the resistivity upon improvement in quasi-crystallinity is discussed in terms of the generalized Faber-Ziman theory and in terms of a possible enhancement in the coherent multiple scattering due to locally well-developed short-range order.
AB The electron transport properties of the thermodynamically stable Al68Cu17Ru15 quasicrystal were studied through the measurements of the electronic sp. heat coeff. and the temp. dependence of the elec. resistivity at 4.2-300 K. The full-width at the half max. for the strongest x-ray diffraction line (100000) is reduced to <0.15 nm-1 either by remelting the ingot with subsequent furnace cooling or by annealing the melt-spun ribbon at 850.degree. for 24 h. An apparent improvement in quasi-crystallinity upon the heat-treatment caused a drastic increase in resistivity up to 1600 .mu..OMEGA. cm and accompanied a very small electronic sp. heat coeff. .gamma. lower then 0.3 mJ mol-1 K-2. The temp. dependence of the resistivity characterized by a concave curvature with a neg. TCR can be discussed in terms of the weak localization of conduction electrons. The thermodynamically stable quasicrystals, like the present Al-Cu-Ru and the previously studied Al-Li-Cu, always exhibit a very low .gamma. value coupled with a high resistivity. The electron d. of states in thermodynamically stable quasicrystal may possess a structure-induced min., and the Fermi level does fall in this crit. range. An increase in the resistivity upon improvement in quasi-crystallinity is discussed in terms of the generalized Faber-Ziman theory and in terms of a possible enhancement in the coherent multiple scattering due to locally well-developed short-range order.

=> s tcr and rtpcr and (J? or M?)
TERM 'M?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED
<------User Break------>
u
SEARCH ENDED BY USER
SEARCH ENDED BY USER
You have entered a truncated stem which occurs in too many terms.
Make the stem longer and try again. For example, if your original term was 'degr?' to search for variations and the abbreviation for 'degradation', you could replace it with the expression '(degrdn OR degrad?)'. If your search term was numeric, e.g., 'C>5', reduce the size of the range.

=> s tcr and rtpcr and oligo?
L5 1 TCR AND RTPCR AND OLIGO?

=> dis l5 ibib abs kwic

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:697109 CAPLUS
DOCUMENT NUMBER: 127:342368
TITLE: Complementary anchor PCR of rearranged variable T-cell receptor .beta.-chain cDNA regions
AUTHOR(S): Oduncu, F.; Krause, G.; Rohnisch, T.; Emmerich, B.; Pachmann, K.
CORPORATE SOURCE: Medizinische Klinik, Klinikum Innenstadt, Munich, D-80336, Germany
SOURCE: Biol. Chem. (1997), 378(10), 1211-1214
CODEN: BICHF3; ISSN: 1431-6730
PUBLISHER: de Gruyter
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sequencible amplificates comprising the variable cDNA sequences of the rearranged T-cell receptor (TCR) .beta.-chain were obtained from the T-leukemia cell line Jurkat using a single-sided PCR approach based on 5 synthetic **oligonucleotides** derived from the flanking const. sequence. Double-stranded cDNA was cleaved by a restriction enzyme creating cohesive ends, to which an anchor **oligonucleotide** was ligated. Since this anchor was complementary to the anti-sense strand of the known const. region, exclusively the desired ligation product folded into a stem-loop-structure that was enzymically extended to yield a PCR template, now flanked at both ends by primer binding sites appropriate for nested PCR.
AB Sequencible amplificates comprising the variable cDNA sequences of the rearranged T-cell receptor (TCR) .beta.-chain were obtained from the T-leukemia cell line Jurkat using a single-sided PCR approach based on 5 synthetic **oligonucleotides** derived from the flanking const.

sequence. Double-stranded cDNA was cleaved by a restriction enzyme creating cohesive ends, to which an anchor **oligonucleotide** was ligated. Since this anchor was complementary to the anti-sense strand of the known const. region, exclusively the desired ligation product folded into a stem-loop-structure that was enzymically extended to yield a PCR template, now flanked at both ends by primer binding sites appropriate for nested PCR.

ST RT PCR **TCR** beta chain cDNA; gene TCRB **RTPCR** JURKAT cell cDNA

IT **TCR** (T cell receptors)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.beta.-chain; complementary anchor PCR of rearranged variable T-cell receptor .beta.-chain cDNA regions)

=> s tcr and rtpcr and oligo and vdj
L6 0 TCR AND RTPCR AND OLIGO AND VDJ

=> s tcr and pcr and vdj
L7 121 TCR AND PCR AND VDJ

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8 48 DUP REM L7 (73 DUPLICATES REMOVED)

=> s l8 and constant
L9 5 L8 AND CONSTANT

=> s l9 1-5 ibib abs kwic
MISSING OPERATOR L9 1-5
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> dis l9 1-5 ibib abs kwic

L9 ANSWER 1 OF 5 MEDLINE
ACCESSION NUMBER: 1999435132 MEDLINE
DOCUMENT NUMBER: 99435132
TITLE: Rearranged T lymphocyte antigen receptor genes as markers of malignant T cells.
AUTHOR: Dreitz M J; Ogilvie G; Sim G K
CORPORATE SOURCE: HESKA Corporation, Ft. Collins, CO 80525, USA.
SOURCE: VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY, (1999 Aug 2) 69 (2-4) 113-9.
Journal code: XCB. ISSN: 0165-2427.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY WEEK: 20000104

AB We have recently cloned a number of canine T cell receptor (**TCR**) Vbeta genes using degenerate oligonucleotides. From the DNA sequences of the resulting clones and the canine Vbeta gene sequences in the literature, seven distinct canine **TCR** Vbeta genes were identified. Vbeta specific **PCR** primers were designed for each of the seven **TCR** Vbeta genes such that under defined conditions, each primer could only amplify a specific **TCR** Vbeta gene in conjunction with the same 3' **constant** region (Cbeta) primer. By performing RT-**PCR** on RNA derived from a source containing T lymphocytes, the presence and expansion of T cells expressing a particular Vbeta gene could be detected. Moreover, the clonality or diversity of a T cell population under analysis could be easily determined by the **VDJ** junctional sequence of the amplified Vbeta **PCR** product, in the form of a "DNA fingerprint". These findings have been used to detect canine T cell lymphoma, and could potentially be used to monitor the remission of T cell malignancies in response to treatment.

AB We have recently cloned a number of canine T cell receptor (**TCR**) Vbeta genes using degenerate oligonucleotides. From the DNA sequences of the resulting clones and the canine Vbeta gene sequences in the literature, seven distinct canine **TCR** Vbeta genes were identified. Vbeta specific **PCR** primers were designed for each of the seven **TCR** Vbeta genes such that under defined conditions, each primer could only amplify a specific **TCR** Vbeta gene in conjunction with the same 3' **constant** region (Cbeta) primer. By performing RT-**PCR** on RNA derived from a source containing T lymphocytes, the presence and expansion of T cells expressing a particular Vbeta. . . be detected. Moreover, the clonality or diversity of a T cell population under analysis could be easily determined by the **VDJ** junctional sequence of the amplified Vbeta **PCR** product, in the form of a "DNA fingerprint". These findings have been used to detect canine T cell lymphoma, and. . .

L9 ANSWER 2 OF 5 MEDLINE
ACCESSION NUMBER: 97378032 MEDLINE
DOCUMENT NUMBER: 97378032
TITLE: Enhancer control of local accessibility to V(D)J recombinase.
AUTHOR: McMurry M T; Hernandez-Munain C; Lauzurica P; Krangel M S
CORPORATE SOURCE: Department of Immunology, Duke University Medical Center, Durham, North Carolina 27710, USA.
CONTRACT NUMBER: GM07071 (NIGMS)
GM41052 (NIGMS)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1997 Aug) 17 (8) 4553-61.
Journal code: NGY. ISSN: 0270-7306.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY WEEK: 19971005

AB We have studied the role of transcriptional enhancers in providing recombination signal sequence (RSS) accessibility to V(D)J recombinase by examining mice carrying a transgenic human T-cell receptor (**TCR**) delta gene minilocus. This transgene is composed of unrearranged variable (Vdelta and Vdelta2), diversity (Ddelta3), joining (Jdeltal and Jdelta3), and **constant** (Cdelta) gene segments. Previous data indicated that with the **TCR** delta enhancer (Edelta) present in the Jdelta3-Cdelta intron, V(D)J recombination proceeds stepwise, first V to D and then VD to J. With the enhancer deleted or mutated, V-to-D rearrangement is intact, but VD-to-J rearrangement is inhibited. We proposed that Edelta is necessary for J segment but not D segment accessibility and that J segment inaccessibility in the enhancerless

minilocus resulted in the observed V(D)J recombination phenotype. In this study, we tested this notion by using ligation-mediated **PCR** to assess the formation of recombination-activating gene (RAG)-dependent double-strand breaks (DSBs) at RSSs 3' of Ddelta3 and 5' of Jdeltal. In five lines of mice carrying multicopy integrants of constructs that either lacked Edelta or carried an inactivated Edelta, the frequency of DSBs 5' of Jdeltal was dramatically reduced relative to that in the wild type, whereas the frequency of DSBs 3' of Ddelta3 was unaffected. We interpret these results to indicate that Edelta is required for Jdeltal but not Ddelta3 accessibility within the minilocus, and we conclude that enhancers regulate V(D)J recombination by providing local accessibility to the recombinase. cis-acting elements other than Edelta must maintain Ddelta3 in an accessible state in the absence of Edelta. The analysis of DSB formation in a single-copy minilocus integrant indicates that efficient DSB formation at the accessible RSS 3' of Ddelta3 requires an accessible partner RSS, arguing that RSS synapsis is required for DSB formation in chromosomal substrates in vivo.

AB . . . enhancers in providing recombination signal sequence (RSS) accessibility to V(D)J recombinase by examining mice carrying a transgenic human T-cell receptor (**TCR**) delta gene minilocus. This transgene is composed of unrearranged variable (Vdelta and Vdelta2), diversity (Ddelta3), joining (Jdeltal and Jdelta3), and **constant** (Cdelta) gene segments. Previous data indicated that with the **TCR** delta enhancer (Edelta) present in the Jdelta3-Cdelta intron, V(D)J recombination proceeds stepwise, first V to D and then VD to. . . . the enhancerless minilocus resulted in the observed V(D)J recombination phenotype. In this study, we tested this notion by using ligation-mediated **PCR** to assess the formation of recombination-activating gene (RAG)-dependent double-strand breaks (DSBs) at RSSs 3' of Ddelta3 and 5' of Jdeltal.. . .

CN EC 2.7.7.- (DNA Nucleotidyltransferases); EC 2.7.7.- (**VDJ** recombinase); 0 (Receptors, Antigen, T-Cell, gamma-delta)

L9 ANSWER 3 OF 5 MEDLINE
ACCESSION NUMBER: 97045028 MEDLINE
DOCUMENT NUMBER: 97045028
TITLE: Cloning of T-cell antigen receptor beta chain cDNAs from Atlantic salmon (Salmo salar).
AUTHOR: Hordvik I; Jacob A L J; Charlemagne J; Endresen C
CORPORATE SOURCE: Department of Fisheries and Marine Biology, High Technology Center University of Bergen, Norway.
SOURCE: IMMUNOGENETICS, (1996) 45 (1) 9-14.
Journal code: GI4. ISSN: 0093-7711.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Cancer Journals; Priority Journals
OTHER SOURCE: GENBANK-X97435
ENTRY MONTH: 199702

AB Atlantic salmon (Salmo salar) cDNAs encoding the T-cell antigen receptor beta chain (TCRB) were isolated from leukocyte RNA by reverse transcription - polymerase chain reaction (RT-**PCR**). Twenty-five distinct cDNA fragments covering the variable (V) - diversity (D) - joining (J) junction and part of the **constant** (C) region were characterized; the sequences of which indicate interchangeable V/D/J usage and expression in the context of one TCRBC gene. Full-length TCRBC sequence information was derived from a leukocyte cDNA library. Key residues of the salmon TCRBC region are in good agreement with those of other species. One distinct exception is the absence of the hinge region cysteine residue which is involved in covalent bonding between the alpha and beta chain in mammalian **TCRs**. As in amphibian and avian species, the salmon TCRBC membrane proximal region is considerably shorter than the mammalian. An octamer sequence (GGACAGGG) very similar to amphibian, avian, and mammalian D sequences could be recognized in the **VDJ** junctions from salmon. The pattern of **VDJ** variability also indicates that mechanisms like trimming and addition occur in fish as in higher vertebrates. Compared with mammals, a relatively high frequency (32%) of the **VDJ** junctions in salmon were out of frame.

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L9 ANSWER 4 OF 5 MEDLINE
ACCESSION NUMBER: 94014793 MEDLINE
DOCUMENT NUMBER: 94014793
TITLE: Ex vivo clonotype primer-directed gene amplification to identify malignant T cell repertoires.
AUTHOR: Beers T; Du T L; Rickert M; Overturf P; Choi Y; Greenberg S J
CORPORATE SOURCE: Department of Neurology, Roswell Park Cancer Institute, Buffalo, NY 14263.
SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (1993 Oct) 54 (4) 343-50.
Journal code: IWY. ISSN: 0741-5400.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199401

AB A novel strategy that utilizes input genomic DNA and overcomes limitations encountered with traditional RNA reverse transcription-polymerase chain reaction (**PCR**) amplification methodology is described to screen for T cell receptor (**TCR**) repertoires. The methodology has been developed to identify individual T cell clonotypes with regard to their unique receptor beta chain variable/diversity/joining (**VDJ**) region gene rearrangement. The technique avoids preselection for a given antigen specificity and is therefore independent of artificial bias introduced by in vitro cell population expansion. This technique was used to detect and identify genetically of malignant clones from heterogeneous mononuclear cell populations from an array of hemato-oncological

disorders, including mycosis fungoides/Sezary Syndrome, adult T cell leukemia, and large granular lymphoproliferative disease. An initial primary PCR, directed by a TCR-J beta generic primer and a complement of family-specific TCR-V beta primers, defines predominant T cell receptor variable gene usage. Use of a TCR-J beta generic primer supplants the use of a constant region primer anchor and thus eliminates the need to target mRNA. The process of variable gene screening also expedites gene sequencing. By sequencing through the VDJ juxtaposed region, i.e., the third complementarity determinant region, clonotype-specific primers are developed and used in a secondary clonotype primer-directed PCR (CPD-PCR) to detect, with extreme sensitivity and specificity, unique T cell clonal repertoires. Analysis of the products of the CPD-PCR permits the detection of a single malignant cell among one million polyclonal cells and supercedes the constraints of prior studies that provide a limited evaluation of family variable gene repertoire usage. This strategy may be applied in the detection of minimal residual disease, in surveillance after induction of disease-free states, and in analyzing the effectiveness of purging autologous bone marrow of malignant clones.

AB A novel strategy that utilizes input genomic DNA and overcomes limitations encountered with traditional RNA reverse transcription-polymerase chain reaction (PCR) amplification methodology is described to screen for T cell receptor (TCR) repertoires. The methodology has been developed to identify individual T cell clonotypes with regard to their unique receptor beta chain variable/diversity/joining (VDJ) region gene rearrangement. The technique avoids preselection for a given antigen specificity and is therefore independent of artificial bias introduced. . . array of hemato-oncological disorders, including mycosis fungoides/Sezary Syndrome, adult T cell leukemia, and large granular lymphoproliferative disease. An initial primary PCR, directed by a TCR-J beta generic primer and a complement of family-specific TCR-V beta primers, defines predominant T cell receptor variable gene usage. Use of a TCR-J beta generic primer supplants the use of a constant region primer anchor and thus eliminates the need to target mRNA. The process of variable gene screening also expedites gene sequencing. By sequencing through the VDJ juxtaposed region, i.e., the third complementarity determinant region, clonotype-specific primers are developed and used in a secondary clonotype primer-directed PCR (CPD-PCR) to detect, with extreme sensitivity and specificity, unique T cell clonal repertoires. Analysis of the products of the CPD-PCR permits the detection of a single malignant cell among one million polyclonal cells and supercedes the constraints of prior studies. . .

L9 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:98766 CAPLUS
DOCUMENT NUMBER: 132:165134
TITLE: Canine T cell receptor .beta.-chain variable regions and their nucleic acids
INVENTOR(S): Dreitz, Matthew J.; Sim, Gek-Kee
PATENT ASSIGNEE(S): Heska Corporation, USA
SOURCE: PCT Int. Appl., 161 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006732	A2	20000210	WO 1999-US17284	19990730
WO 2000006732	A3	20000504		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9952444	A1	20000221	AU 1999-52444	19990730
WO 2001007616	A1	20010201	WO 2000-US6742	20000310
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:
US 1998-94930 19980731
US 1999-359084 19990722
WO 1999-US17284 19990730
US 1999-447399 19991123

AB The present invention provides for isolated T cell receptor .beta.-chain variable region (TCRV.beta.) proteins, isolated TCR V.beta. nucleic acid mols., antibodies directed against TCR V.beta. proteins, and compds. derived therefrom that regulate the immune response response of an animal. Seven different V.beta. isoforms from Canis familiaris and their cDNA sequences are provided. The sequences are useful for detection of expansion of T cells and for the diagnosis and treatment of TCR-assocd. diseases.

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ST TCR receptor beta chain cDNA sequence dog

IT Allergy inhibitors
Anti-infective agents
Antiasthmatics
Antibacterial agents
Antidiabetic agents
Antirheumatic agents
Antitumor agents
Antiviral agents
Dog (Canis familiaris)
PCR (polymerase chain reaction)
Parasiticides

Vaccines
(canine T cell receptor .beta.-chain variable regions and their nucleic acids)

IT TCR (T cell receptors)
RL: ARG (Analytical reagent use); BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(canine T cell receptor .beta.-chain variable regions and their nucleic acids)

IT cDNA sequences
(for canine T cell receptor .beta.-chain VDJ regions)

IT Protein sequences
(of canine T cell receptor .beta.-chain VDJ regions)

IT 258323-08-9 258323-09-0 258323-10-3 258323-11-4 258323-12-5
258323-13-6 258323-14-7 258323-15-8 258323-16-9 258325-19-8
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer for const. region; canine T cell receptor .beta.-chain variable regions and their nucleic acids)

=> dis his

(FILE 'HOME' ENTERED AT 10:44:33 ON 18 APR 2001)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 10:44:42 ON 18 APR 2001
L1 0 S MJ? AND TCR AND (RTPCR OR PCR)
L2 0 S MJ? AND APLPHA
L3 6 S MJ? AND TCR
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)
L5 1 S TCR AND RTPCR AND OLIGO?
L6 0 S TCR AND RTPCR AND OLIGO AND VDJ
L7 121 S TCR AND PCR AND VDJ
L8 48 DUP REM L7 (73 DUPLICATES REMOVED)
L9 5 S L8 AND CONSTANT

=> s ((primer? (5N) (Valpha or Vbeta)) and TCR
UNMATCHED LEFT PARENTHESIS '((PRIMER?'
The number of right parentheses in a query must be equal to the number of left parentheses.

=> s ((primer? (5N) (Valpha or Vbeta))) and TCR
L10 17 ((PRIMER? (5N) (VALPHA OR VBETA))) AND TCR

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11 12 DUP REM L10 (5 DUPLICATES REMOVED)

=> dis l11 1-12 kwic

L11 ANSWER 1 OF 12 MEDLINE
AB The T-cell receptor (**TCR**) CDR3 length heterogeneity is formed during recombination of individual Vbeta gene families. We hypothesized that CDR3 length diversity could be used to assess the fundamental differences within the **TCR** repertoire of CD45RA and CD45RO T-cell subpopulations. By using PCR-based spectratyping, nested **primers** for all 24 human **Vbeta** families were developed to amplify CDR3 lengths in immunomagnetically selected CD45RA and CD45RO subsets within both CD4(+) and CD8(+) T-cell. . . . of the CDR3 length diversity within CD45RA and CD45RO T cells provides a more accurate measure of disturbances in the **TCR** repertoire than analysis of unfractionated CD4 and CD8 T cells.

L11 ANSWER 2 OF 12 MEDLINE DUPLICATE 1
AB . . . in the peripheral blood, liver, and spleen of Patient 2. In the two patients, T-cell receptor-beta and alpha-chain variable region (**TCR** Vbeta and V alpha) repertoires in peripheral mononuclear cells were analyzed at the time of disease onset and at disease. . . of a specific Vbeta family member was observed, a clonal analysis was performed by PCR using beta-chain joining region (Jbeta) **primers**. The clonality of specific **Vbeta**-Jbeta fragments was confirmed by a single strand confirmation polymorphism (SSCP) analysis. RESULTS: Although there was no preferential usage of Vbeta. . .

L11 ANSWER 3 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
AB The examination of T-cell receptor (**TCR**) repertoires has an important role in the study of lymphoproliferative disorders and autoimmune diseases. Analysis of the complementarity-determining region 3 (CDR3) of the **TCR** beta chain is used to assess the clonality of T-cell populations. We developed a rapid fluorescence-based method for CDR3 length analysis of expressed **TCR** gene families. **TCR** beta chain complementary DNA is amplified by a nested polymerase chain reaction with **Vbeta** family-specific oligonucleotide **primers** and a fluorochrome-labeled Cbeta primer. The polymerase chain reaction products were analyzed on a compact automated DNA sequencing system (OpenGene. . .

L11 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
AB. . . T-cell trigger and is determined by a T-cell driven immune response, and to assess the clonality of CD4+ and CD8+ **TcR** usage in subjects with FASSc. Materials and methods We used reverse transcription polymerase chain reaction with specific **Valpha**- and **Vbeta**-chain **primers** to identify the **TcR** gene usage in biopsy material, bronchoalveolar lavage fluid or peripheral blood from our subjects. Results We found individual-specific restriction of. . . between lung and peripheral blood lymphocyte Vbeta-families in CD8+ T-cells (P = 0.0007). Conclusion We conclude that there is individual **TcR** Valpha- and Vbeta-expression bias in subjects with fibrosing alveolitis.

L11 ANSWER 5 OF 12 MEDLINE DUPLICATE 2
AB We have recently cloned a number of canine T cell receptor (**TCR**) Vbeta genes using degenerate oligonucleotides. From the DNA sequences of the resulting clones and the canine Vbeta gene sequences in the literature, seven distinct canine **TCR** Vbeta genes were identified. **Vbeta** specific PCR **primers** were designed for each of the seven **TCR** Vbeta genes such that under defined conditions, each primer could only amplify a specific **TCR** Vbeta gene in conjunction with the same 3' constant region (Cbeta) primer. By performing RT-PCR on RNA derived from a. . .

L11 ANSWER 6 OF 12 MEDLINE DUPLICATE 3
AB . . . lines previously established with interleukin-2 (IL-2) and IL-7

from the skin and from the blood. Analysis of the T-cell receptor (TCR) Vbeta gene expression showed that the tumor cells, which were shown to have a trisomy 7 by fluorescent in situ. . . monoclonal antibodies indicated that only Vbeta13 could be detected on the cell membrane of the tumor cells. Analysis of the TCR Vbeta gene expression of the clones showed that TC5 and TC7 expressed a unique TCR-Vbeta transcript, corresponding, respectively, to Vbeta5/Jbeta2.3 and Vbeta17/Jbeta2.7 gene segments. To determine whether these reactive T lymphocytes were present in vivo, we used specific **primers** corresponding to TC5- and TC7-**Vbeta** TCR transcripts. The results showed that both cytotoxic T-cell clones were present at the lesional skin site and amplified in vitro.. . .

L11 ANSWER 7 OF 12 MEDLINE DUPLICATE 4
TI TCR-Vbeta usage in the thymus and blood of myasthenia gravis patients.
AB . . . to whether sAg play a role in the pathogenesis of MG. We investigated the frequency of use of the different TCR Vbeta families by the thymus and blood T cells in MG patients and in control subjects, using a multi-**primer** PCR assay. Identical TCR -**Vbeta** usage was found in the thymi of MG patients and controls, except Vbeta2, which showed a small increase in MG. . . the immunodominance of certain AChR epitopes, or the action of a sAg outside the thymus. The minimal differences in the TCR-Vbeta usage in the blood and thymus of control subjects might be due to expansion of T cell clones specific for. . .

L11 ANSWER 8 OF 12 MEDLINE
AB . . . clinical application of such analyses has been limited. Here we have established novel primers to anneal with T cell receptor (TCR) beta genes of multiple Vbeta families and applied them to reverse transcription-polymerase chain reaction-single strand conformation polymorphism (RT-PCR-SSCP) analysis to evaluate peripheral T cell clonality of autoimmune disease patients. As a result, the new **Vbeta primers** could detect accumulating T cell clones in the periphery of healthy individuals and patients. It was revealed that patients with. . . number of clonal accumulations of peripheral T cells compared with normal individuals. Thus, the RT-PCR-SSCP system using the new multifamily **Vbeta primers** is the first such laboratory examination to detect T cell clonal expansion, and will provide a simple and sensitive tool. . .

L11 ANSWER 9 OF 12 MEDLINE DUPLICATE 5
AB . . . patients with toxic liver injury were extracted and analysed using a semiquantitative RT-PCR with a panel of T cell receptor **Vbeta** family specific **primers**. After agarose gel electrophoresis, the distribution of T cell receptor (TCR) Vbeta molecules was assessed by densitometry. Furthermore, results were compared to the TCR Vbeta distribution of 10 healthy blood donors. RESULTS: Four of 12 patients with untreated autoimmune hepatitis but no patients with chronic hepatitis C and toxic liver injury showed a significant overexpression of TCR Vbeta3 (17.8% +/- 2.6% vs. 9.3% +/- 4.6%; p = 0.01) and three an overexpression of Vbeta13.1 (14.6% +/- 2.3% vs. 6.6% +/- 3.5%; p = 0.02) molecules compared to the TCR Vbeta-distribution in healthy blood donors. In addition, Vbeta3+ T cells were found enriched in the liver tissue compared to autologous. . . in the liver tissue from one of three patients with overexpression. CONCLUSIONS: In autoimmune hepatitis a disease specific compartmentalisation of TCR Vbeta3+ T cells was observed in the liver tissues. Although their specificity was unknown, this might indicate that these infiltrating. . .

L11 ANSWER 10 OF 12 MEDLINE
TI TCR vbeta usage of TSH receptor-specific CD4+ T cells in Graves' disease patients and healthy humans.
AB . . . have CD4+ T cells specific for self-components. Since autoreactive T cells in autoimmune patients may use a limited number of TCR V-region genes, we investigated here whether this also occurs for the potentially autoreactive CD4+ cells present in healthy persons. We. . . repertoire had been characterized previously: each line recognized one or a few TSHr peptides, different for each subject.We determined their TCR Vbeta usage by a semi-quantitative reverse transcriptase PCR assay, using **primers** specific for each known human **Vbeta** region family, in conjunction with a constant region **primer**. Six lines preferentially used one **Vbeta** family (42-94%), different for each line. In all lines, three or less Vbeta families accounted for approximately 60% or more. . . CD4+ cells involved in autoimmune diseases are likely recruited from that pool, since they have similar characteristics of epitope and TCR repertoire as the CD4+ cells specific for the same autoantigen in healthy subjects.

L11 ANSWER 11 OF 12 MEDLINE
AB . . . was employed to examine T cells in middle ear effusions in patients with OME for utilization of T cell receptor (TCR) variable region genes. Specimens of RNA were extracted from 13 ears of 12 patients (9 children and 3 adults). Oligonucleotide **primers** specific for individual TCR **Vbeta** gene families were used to amplify TCR gene products in each sample. Although the number of Vbeta families utilized by each sample varied from 1 family to. . .

L11 ANSWER 12 OF 12 MEDLINE
AB We analyzed the T-cell repertoire in patients transplanted with bone marrow from an HLA identical sibling by determining the TCR diversity through Vbeta-CDR3-size spectratyping with **Vbeta** /Cbeta- and **Vbeta**/Jbeta-specific **primers**. Using the **Vbeta**/Cbeta **primers**, we observed limited TCR diversity only in recipients of a T-cell-depleted graft, whereas the TCR diversity of patients transplanted with an unmanipulated graft seemed to be indistinguishable from the one of a normal individual. However, with **Vbeta**/Jbeta-specific **primers**, increase of the resolution by approximately 10-fold also allowed the detection of imbalances in the TCR repertoire of recipients of an unmanipulated graft. This demonstrates that when high numbers of T cells are cotransfused with marrow, the TCR repertoire is more complete but still not as complete as in normal individuals, thereby emphasizing the important role of coinfused. . .

=> dis l11 1-12 ibib abs

L11 ANSWER 1 OF 12 MEDLINE

ACCESSION NUMBER: 2001136996 MEDLINE
DOCUMENT NUMBER: 20517578
TITLE: T-Cell receptor Vbeta repertoire CDR3 length diversity differs within CD45RA and CD45RO T-cell subsets in healthy and human immunodeficiency virus-infected children.
AUTHOR: Kou Z C; Puhr J S; Rojas M; McCormack W T; Goodenow M M; Sleasman J W
CORPORATE SOURCE: Department of Pediatrics, Division of Immunology and Infectious Diseases, University of Florida College of Medicine, Gainesville, Florida 32610-0296, USA.
CONTRACT NUMBER: RO1 HD32259 (NICHD)
RO1 HL58005 (NHLBI)
RR0082 (NCRR)
SOURCE: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, (2000 Nov) 7 (6) 953-9.
Journal code: CB7. ISSN: 1071-412X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
AB The T-cell receptor (**TCR**) CDR3 length heterogeneity is formed during recombination of individual Vbeta gene families. We hypothesized that CDR3 length diversity could be used to assess the fundamental differences within the **TCR** repertoire of CD45RA and CD45RO T-cell subpopulations. By using PCR-based spectratyping, nested **primers** for all 24 human **Vbeta** families were developed to amplify CDR3 lengths in immunomagnetically selected CD45RA and CD45RO subsets within both CD4(+) and CD8(+) T-cell populations. Umbilical cord blood mononuclear cells or peripheral blood mononuclear cells obtained from healthy newborns, infants, and children, as well as human immunodeficiency virus (HIV)-infected children, were analyzed. All T-cell subsets from newborn and healthy children demonstrated a Gaussian distribution of CDR3 lengths in separated T-cell subsets. In contrast, HIV-infected children had a high proportion of predominant CDR3 lengths within both CD45RA and CD45RO T-cell subpopulations, most commonly in CD8(+) CD45RO T cells. Sharp differences in clonal dominance and size distributions were observed when cells were separated into CD45RA or CD45RO subpopulations. These differences were not apparent in unfractionated CD4(+) or CD8(+) T cells from HIV-infected subjects. Sequence analysis of predominant CDR3 lengths revealed oligoclonal expansion within individual Vbeta families. Analysis of the CDR3 length diversity within CD45RA and CD45RO T cells provides a more accurate measure of disturbances in the **TCR** repertoire than analysis of unfractionated CD4 and CD8 T cells.

L11 ANSWER 2 OF 12 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999208300 MEDLINE
DOCUMENT NUMBER: 99208300
TITLE: Clonal change of infiltrating T-cells in children with familial hemophagocytic lymphohistiocytosis: possible association with Epstein-Barr virus infection.
AUTHOR: Ishii E; Kimura N; Kato K; Sako M; Nagano M; Nakagawa A; Okamura T; Yamaguchi H; Kawa K; Hara T
CORPORATE SOURCE: Division of Pediatrics, Hamanomachi Hospital, Fukuoka, Japan.
SOURCE: CANCER, (1999 Apr 1) 85 (7) 1636-43.
Journal code: CLZ. ISSN: 0008-543X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199907
ENTRY WEEK: 19990702
AB BACKGROUND: Although familial hemophagocytic lymphohistiocytosis (FHL) has been considered a T-cell disorder, to the authors' knowledge there are no previous reports on the clonal basis of FHL. In the current study the authors analyzed the clonality of T-cells in two FHL patients at the time of disease onset and at disease progression. METHODS: Patient 1 had FHL and died of recurrent disease 4 months after bone marrow transplantation (BMT). His liver and spleen showed massive infiltrations of CD3+, CD4-, and CD8+ T-cells. The Epstein-Barr virus (EBV) genome was detected by in situ hybridization. Patient 2 also had FHL and died of progressive disease 9 weeks after the onset of disease despite chemotherapy. A polymerase chain reaction (PCR) analysis showed positive EBV genome in the peripheral blood, liver, and spleen of Patient 2. In the two patients, T-cell receptor-beta and alpha-chain variable region (**TCR** Vbeta and V alpha) repertoires in peripheral mononuclear cells were analyzed at the time of disease onset and at disease progression by the inverse PCR method. When a high usage (> 15%) of a specific Vbeta family member was observed, a clonal analysis was performed by PCR using beta-chain joining region (Jbeta) **primers**. The clonality of specific **Vbeta** -Jbeta fragments was confirmed by a single strand confirmation polymorphism (SSCP) analysis. RESULTS: Although there was no preferential usage of Vbeta in Patient 1, the exclusive expression of Jbeta1.2 for Vbeta13 was observed. A high frequency of Vbeta13 also was observed at the time of disease progression, but the Jbeta fragment for Vbeta13 was polyclonal. In Patient 2, the restricted usage of Jbeta1.6 for Vbeta5a was observed at the time of disease onset, whereas Jbeta1.1 and 1.2 for Vbeta4 were observed exclusively at the time of disease progression. The clonality of Vbeta13-Jbeta1.2 in Patient 1 and Vbeta5a-Jbeta1.6 and Vbeta4-Jbeta1.1/Jbeta1.2 in Patient 2 was confirmed by SSCP analysis. CONCLUSIONS: These findings suggest that the polyclonal T-cell lymphoproliferative disease associated with EBV was induced after BMT in Patient 1, and that the clonal change of expanded T-cells also was induced by EBV in Patient 2. The clonal analysis of T-cells is a useful tool to clarify the pathogenesis of FHL.

L11 ANSWER 3 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:256318 BIOSIS
DOCUMENT NUMBER: PREV199900256318
TITLE: An automated method for the analysis of T-cell receptor repertoires: Rapid RT-PCR fragment length analysis of the T-cell receptor beta chain complementarity-determining region 3.
AUTHOR(S): Lue, Cummins (1); Mitani, Yuichi; Crew, Mark D.; George, James F.; Fink, Louis M.; Schichman, Steven A.
CORPORATE SOURCE: (1) Department of Medicine, University of Arkansas for Medical Sciences, 4301 West Markham, Slot 509, Little Rock, AR, 72205 USA
SOURCE: American Journal of Clinical Pathology, (May, 1999) Vol. 111, No. 5, pp. 683-690.

ISSN: 0002-9173.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The examination of T-cell receptor (**TCR**) repertoires has an important role in the study of lymphoproliferative disorders and autoimmune diseases. Analysis of the complementarity-determining region 3 (CDR3) of the **TCR** beta chain is used to assess the clonality of T-cell populations. We developed a rapid fluorescence-based method for CDR3 length analysis of expressed **TCR** gene families. **TCR** beta chain complementary DNA is amplified by a nested polymerase chain reaction with **Vbeta** family-specific oligonucleotide **primers** and a fluorochrome-labeled Cbeta primer. The polymerase chain reaction products were analyzed on a compact automated DNA sequencing system (OpenGene system, Visible Genetics, Toronto, Ontario). To demonstrate the usefulness of our technique, we examined the CDR3 length distribution of peripheral blood T cells from a healthy subject, intestinal T cells from a patient with ulcerative colitis, and the T-cell leukemia cell line Jurkat. The analysis revealed polyclonal, oligoclonal, and monoclonal CDR3 distributions, respectively, for the 3 T-cell populations. Our new method shows virtually identical CDR3 length patterns compared with the traditional radioisotope-based method. The new technique offers the convenience of rapid throughput, nonradioactive labeling, and quality data analysis.

L11 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:195044 BIOSIS
DOCUMENT NUMBER: PREV199900195044
TITLE: T-cell receptor gene usage in patients with fibrosing alveolitis and control subjects.
AUTHOR(S): Lympany, P. A.; Southcott, A. M.; Welsh, K. I.; Black, C. M.; Boylston, A. W.; du Bois, R. M. (1)
CORPORATE SOURCE: (1) Interstitial Lung Disease Unit, Department of Occupational and Environmental Medicine, Imperial College of Science, Technology and Medicine, 1B Manresa Road, Emmanuel Kaye Building, London, SW3 6LR UK
SOURCE: European Journal of Clinical Investigation, (Feb., 1999) Vol. 29, No. 2, pp. 173-181.
ISSN: 0014-2972.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Background Fibrosing alveolitis is characterized by inflammation, fibrosis and increased numbers of activated CD4+ T-cells in the lower respiratory tract. The aims of this study were to compare the T-cell antigen receptor repertoire in the lungs of subjects with fibrosing alveolitis systemic sclerosis (FASSc) with cryptogenic fibrosing alveolitis (CFA) and normal control subjects, to determine whether FASSc is driven by a specific T-cell trigger and is determined by a T-cell driven immune response, and to assess the clonality of CD4+ and CD8+ **TcR** usage in subjects with FASSc. Materials and methods We used reverse transcription polymerase chain reaction with specific **Valpha**- and **Vbeta**-chain **primers** to identify the **TcR** gene usage in biopsy material, bronchoalveolar lavage fluid or peripheral blood from our subjects. Results We found individual-specific restriction of Valpha- and Vbeta-chain usage in lung biopsies from patients and control subjects. To establish whether this was due to expression bias in the CD4+ or CD8+ T-cells and was restricted to the lung, the alphabeta-T-cell receptor chain usage was assessed in T-cell subsets separated from the lungs of patients with fibrosing alveolitis and was compared with that of the peripheral blood. There was no consistent difference in the expression of any variable family chain among the population studied, although there was a significant difference between lung and peripheral blood lymphocyte Vbeta-families in CD8+ T-cells ($P = 0.0007$). Conclusion We conclude that there is individual **TcR** Valpha- and Vbeta-expression bias in subjects with fibrosing alveolitis.

L11 ANSWER 5 OF 12 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1999435132 MEDLINE
DOCUMENT NUMBER: 99435132
TITLE: Rearranged T lymphocyte antigen receptor genes as markers of malignant T cells.
AUTHOR: Dreitz M J; Ogilvie G; Sim G K
CORPORATE SOURCE: HESKA Corporation, Ft. Collins, CO 80525, USA.
SOURCE: VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY, (1999 Aug 2) 69 (2-4) 113-9.
Journal code: XCB. ISSN: 0165-2427.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY WEEK: 20000104
AB We have recently cloned a number of canine T cell receptor (**TCR**) Vbeta genes using degenerate oligonucleotides. From the DNA sequences of the resulting clones and the canine Vbeta gene sequences in the literature, seven distinct canine **TCR** Vbeta genes were identified. **Vbeta** specific PCR **primers** were designed for each of the seven **TCR** Vbeta genes such that under defined conditions, each primer could only amplify a specific **TCR** Vbeta gene in conjunction with the same 3' constant region (Cbeta) primer. By performing RT-PCR on RNA derived from a source containing T lymphocytes, the presence and expansion of T cells expressing a particular Vbeta gene could be detected. Moreover, the clonality or diversity of a T cell population under analysis could be easily determined by the VDJ junctional sequence of the amplified Vbeta PCR product, in the form of a "DNA fingerprint". These findings have been used to detect canine T cell lymphoma, and could potentially be used to monitor the remission of T cell malignancies in response to treatment.

L11 ANSWER 6 OF 12 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1998261461 MEDLINE
DOCUMENT NUMBER: 98261461
TITLE: Isolation of tumor-specific cytotoxic CD4+ and CD4+CD8dim+ T-cell clones infiltrating a cutaneous T-cell lymphoma.
AUTHOR: Bagot M; Echchakir H; Mami-Chouaib F; Delfau-Larue M H; Charue D; Bernheim A; Chouaib S; Boumsell L; Bensussan A
CORPORATE SOURCE: INSERM U448, Paris XII University, Paris, France.
SOURCE: BLOOD, (1998 Jun 1) 91 (11) 4331-41.
Journal code: A8G. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer

Journals
ENTRY MONTH: 199809
ENTRY WEEK: 19980901
AB We have isolated several T-cell clones from lymphocytes infiltrating a human major histocompatibility class (MHC) II negative cutaneous T-cell lymphoma (CTCL). We describe here two of these clones, TC5 and TC7, with, respectively, a CD4(+)CD8dim+ and CD4(+)CD8(-) phenotype. Both clones mediated a specific MHC class I-restricted cytotoxic activity toward the fresh autologous tumor cells, and autologous tumor cell lines previously established with interleukin-2 (IL-2) and IL-7 from the skin and from the blood. Analysis of the T-cell receptor (**TCR**) Vbeta gene expression showed that the tumor cells, which were shown to have a trisomy 7 by fluorescent in situ hybridization, expressed Vbeta7/Jbeta2.3, Vbeta13/Jbeta2.5, and Vbeta22/Jbeta2.5 rearrangements. Phenotypic analysis using specific anti-Vbeta monoclonal antibodies indicated that only Vbeta13 could be detected on the cell membrane of the tumor cells. Analysis of the **TCR** Vbeta gene expression of the clones showed that TC5 and TC7 expressed a unique **TCR**-Vbeta transcript, corresponding, respectively, to Vbeta5/Jbeta2.3 and Vbeta17/Jbeta2.7 gene segments. To determine whether these reactive T lymphocytes were present in vivo, we used specific **primers** corresponding to TC5- and TC7-**Vbeta TCR** transcripts. The results showed that both cytotoxic T-cell clones were present at the lesional skin site and amplified in vitro. TC7 was found in the patient peripheral blood invaded by tumoral cells, whereas TC5 was not, indicating that the repertoire of the reactional lymphocytes differs in the blood and at the tumor site. These results show for the first time the presence of reactive T lymphocytes with CD4 or double-positive phenotype infiltrating a CTCL. These findings raise the question of the role of these antitumoral effector T cells in the tumor growth.

L11 ANSWER 7 OF 12 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1999096524 MEDLINE
DOCUMENT NUMBER: 99096524
TITLE: **TCR**-Vbeta usage in the thymus and blood of myasthenia gravis patients.
AUTHOR: Navaneetham D; Penn A S; Howard JFJr; Conti-Fine B M
CORPORATE SOURCE: College of Biological Sciences, University of Minnesota, St. Paul, MN, 55108, USA.
CONTRACT NUMBER: NS 23919 (NINDS)
NS 17904 (NINDS)
SOURCE: JOURNAL OF AUTOIMMUNITY, (1998 Dec) 11 (6) 621-33.
Journal code: ADL. ISSN: 0896-8411.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY WEEK: 19990402
AB In myasthenia gravis (MG) the muscle acetylcholine receptor (AChR) is the target of an autoimmune response. The anti-AChR response may originate in the thymus, which is abnormal in most MG patients and contains anti-AChR T and B cells. Microbial superantigens (sAg) may trigger autoimmune responses and in this study we sought clues as to whether sAg play a role in the pathogenesis of MG. We investigated the frequency of use of the different **TCR** Vbeta families by the thymus and blood T cells in MG patients and in control subjects, using a multi-**primer** PCR assay. Identical **TCR-Vbeta** usage was found in the thymi of MG patients and controls, except Vbeta2, which showed a small increase in MG patients' thymi. Blood T cells of MG patients used Vbeta4, Vbeta6, Vbeta15, Vbeta16 and Vbeta24 significantly more than those of the controls. Vbeta4 and Vbeta6 are the gene families most frequently used by anti-AChR CD4(+) cells in MG patients. Blood T cells from MG patients used Vbeta12, Vbeta14, Vbeta17 and Vbeta18 significantly less than controls. MG patients used Vbeta4 and Vbeta6 significantly more in the blood than in the thymus, while the opposite occurred for Vbeta7, Vbeta12 and Vbeta14. Controls used Vbeta17 more and Vbeta24 less in the blood than in the thymus. The preferential expansion of Vbeta4 and Vbeta6 in MG patients might reflect the immunodominance of certain AChR epitopes, or the action of a sAg outside the thymus. The minimal differences in the **TCR**-Vbeta usage in the blood and thymus of control subjects might be due to expansion of T cell clones specific for common antigens. Identical Vbeta usage in the thymi of MG patients and controls does not support an important role of the thymus as the location of anti-AChR sensitization when MG is clinically evident. The differences observed in the Vbeta usage in blood and thymi of MG patients are likely to be due to preferential Vbeta usage by the anti-AChR T cells in the blood. Copyright 1998 Academic Press

L11 ANSWER 8 OF 12 MEDLINE
ACCESSION NUMBER: 1998252377 MEDLINE
DOCUMENT NUMBER: 98252377
TITLE: Frequent clonal expansion of peripheral T cells in patients with autoimmune diseases: a novel detecting system possibly applicable to laboratory examination.
AUTHOR: Masuko-Hongo K; Kato T; Suzuki S; Sekine T; Kurokawa M; Ueda S; Yamada A; Nishioka K; Yamamoto K
CORPORATE SOURCE: Rheumatology, Immunology and Genetics Program, Institute of Medical Sciences, St. Marianna University, Kanagawa, Japan.. GBH01723@niftyserve.or.jp
SOURCE: JOURNAL OF CLINICAL LABORATORY ANALYSIS, (1998) 12 (3) 162-7.
Journal code: JLA. ISSN: 0887-8013.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY WEEK: 19980901
AB To investigate T cell involvement in antigen-specific immune responses, it is important to detect accumulating T cells at a clonal level in vivo. However, thus far the clinical application of such analyses has been limited. Here we have established novel primers to anneal with T cell receptor (**TCR**) beta genes of multiple Vbeta families and applied them to reverse transcription-polymerase chain reaction-single strand conformation polymorphism (RT-PCR-SSCP) analysis to evaluate peripheral T cell clonality of autoimmune disease patients. As a result, the new **Vbeta primers** could detect accumulating T cell clones in the periphery of healthy individuals and patients. It was revealed that patients with autoimmune diseases such as systemic lupus erythematosus (SLE) had a larger number of clonal accumulations of peripheral T cells compared with normal individuals. Thus, the RT-PCR-SSCP system using the new multifamily **Vbeta primers** is the first such

laboratory examination to detect T cell clonal expansion, and will provide a simple and sensitive tool to aid in the diagnosis and also in the investigation of the pathogenesis of autoimmune diseases.

L11 ANSWER 9 OF 12 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1998140913 MEDLINE
DOCUMENT NUMBER: 98140913
TITLE: Limited T cell receptor Vbeta-chain repertoire of liver-infiltrating T cells in autoimmune hepatitis.
AUTHOR: Arenz M; Meyer zum Buschenfelde K H; Lohr H F
CORPORATE SOURCE: Ist. Dept. of Internal Medicine, Johannes Gutenberg-University, Mainz, Germany.
SOURCE: JOURNAL OF HEPATOLOGY, (1998 Jan) 28 (1) 70-7. Journal code: IBS. ISSN: 0168-8278.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY WEEK: 19980602
AB BACKGROUND/AIMS: To characterize the cellular immune reactions in autoimmune hepatitis, the T cell receptor repertoire of liver-infiltrating and circulating T cells was studied. METHODS: Nucleic acids of liver-tissue and peripheral blood-derived T cells from 12 patients with untreated autoimmune hepatitis, four patients with chronic hepatitis C and three patients with toxic liver injury were extracted and analysed using a semiquantitative RT-PCR with a panel of T cell receptor **Vbeta** family specific **primers**. After agarose gel electrophoresis, the distribution of T cell receptor (**TCR**) Vbeta molecules was assessed by densitometry. Furthermore, results were compared to the **TCR** Vbeta distribution of 10 healthy blood donors. RESULTS: Four of 12 patients with untreated autoimmune hepatitis but no patients with chronic hepatitis C and toxic liver injury showed a significant overexpression of **TCR** Vbeta3 (17.8% +/- 2.6% vs. 9.3% +/- 4.6%; p = 0.01) and three an overexpression of Vbeta13.1 (14.6% +/- 2.3% vs. 6.6% +/- 3.5%; p = 0.02) molecules compared to the **TCR** Vbeta-distribution in healthy blood donors. In addition, Vbeta3+ T cells were found enriched in the liver tissue compared to autologous peripheral blood in three autoimmune hepatitis patients (15.3% +/- 7.0% vs. 5.2% +/- 3.1%; L/B ratio: 2.9), while Vbeta13.1+ T cells were enriched in the liver tissue from one of three patients with overexpression. CONCLUSIONS: In autoimmune hepatitis a disease specific compartmentalisation of **TCR** Vbeta3+ T cells was observed in the liver tissues. Although their specificity was unknown, this might indicate that these infiltrating T cells could have relevance for abnormal immunoregulation.

L11 ANSWER 10 OF 12 MEDLINE
ACCESSION NUMBER: 1998018742 MEDLINE
DOCUMENT NUMBER: 98018742
TITLE: **TCR** vbeta usage of TSH receptor-specific CD4+ T cells in Graves' disease patients and healthy humans.
AUTHOR: Raju R; Navaneetham D; Kellermann S A; Freeman S L; Morris J C; McCormick D J; Conti-Fine B M
CORPORATE SOURCE: Department of Biochemistry, University of Minnesota, St Paul, MN 55108, USA.
CONTRACT NUMBER: NS 23919 (NINDS)
SOURCE: JOURNAL OF AUTOIMMUNITY, (1997 Oct) 10 (5) 479-89. Journal code: ADL. ISSN: 0896-8411.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY WEEK: 19980104
AB Healthy humans have CD4+ T cells specific for self-components. Since autoreactive T cells in autoimmune patients may use a limited number of **TCR** V-region genes, we investigated here whether this also occurs for the potentially autoreactive CD4+ cells present in healthy persons. We studied CD4+ cells specific for human TSH receptor (TSHr) sequences, that are present with high frequency in healthy subjects and, as expected, in Graves' disease (GD) patients. We used short-term CD4+ cell lines propagated from four GD patients and five healthy subjects by cycles of stimulation with a pool of overlapping synthetic peptides corresponding to the putative extracellular parts of the TSHr sequence. The lines recognized the pool of TSHr peptides specifically and vigorously. Their epitope repertoire had been characterized previously: each line recognized one or a few TSHr peptides, different for each subject.We determined their **TCR** Vbeta usage by a semi-quantitative reverse transcriptase PCR assay, using **primers** specific for each known human **Vbeta** region family, in conjunction with a constant region **primer**. Six lines preferentially used one **Vbeta** family (42-94%), different for each line. In all lines, three or less Vbeta families accounted for approximately 60% or more of the Vbeta usage. Different Vbeta regions were used by each subject. There was no obvious difference between the Vbeta usage of the lines from GD patients and healthy controls.These results suggest that a limited pool of potentially autoreactive T cells survives clonal deletion. The pathogenic CD4+ cells involved in autoimmune diseases are likely recruited from that pool, since they have similar characteristics of epitope and **TCR** repertoire as the CD4+ cells specific for the same autoantigen in healthy subjects. Copyright 1997 Academic Press Limited.

L11 ANSWER 11 OF 12 MEDLINE
ACCESSION NUMBER: 96202866 MEDLINE
DOCUMENT NUMBER: 96202866
TITLE: Analysis of T cell receptor beta chain repertoire in middle ear effusions.
AUTHOR: Takeuchi K; Fujita Y; Tomemori T; Yuta A; Iriyoshi N; Sakakura Y
CORPORATE SOURCE: Department of Otorhinolaryngology, Mie University School of Medicine, Tsu, Japan.
SOURCE: ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, (1996 Mar) 105 (3) 213-7. Journal code: 5Q2. ISSN: 0003-4894.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199608
AB In order to elucidate the immune response in otitis media with effusion (OME), the polymerase chain reaction was employed to examine T cells in middle ear effusions in patients with OME for utilization of T cell receptor (**TCR**) variable region genes. Specimens of RNA were

extracted from 13 ears of 12 patients (9 children and 3 adults). Oligonucleotide **primers** specific for individual **TCR** **Vbeta** gene families were used to amplify **TCR** gene products in each sample. Although the number of Vbeta families utilized by each sample varied from 1 family to 21, a few significant trends emerged. Eleven ears out of 13 expressed Vbeta7, which was the most frequently utilized (84.6%) Vbeta family among the 24 Vbeta families. In 5 of the 13 samples, the number of Vbeta families utilized was restricted to 1, which was Vbeta7 in all 5 samples. This result indicates the possibility that Vbeta7-bearing T cells in the middle ear are responding to a certain common antigen in some cases of OME.

L11 ANSWER 12 OF 12 MEDLINE
ACCESSION NUMBER: 96421965 MEDLINE
DOCUMENT NUMBER: 96421965
TITLE: T-cell repertoire complexity after allogeneic bone marrow transplantation.
AUTHOR: Roux E; Helg C; Chapuis B; Jeannet M; Roosnek E
CORPORATE SOURCE: Division of Immunology, Department of Internal Medicine, Hopital Cantonal Universitaire, Geneva, Switzerland.
SOURCE: HUMAN IMMUNOLOGY, (1996 Jun-Jul) 48 (1-2) 135-8. Journal code: G9W. ISSN: 0198-8859.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY WEEK: 19970402
AB We analyzed the T-cell repertoire in patients transplanted with bone marrow from an HLA identical sibling by determining the **TCR** diversity through Vbeta-CDR3-size spectratyping with **Vbeta** /Cbeta- and **Vbeta**/Jbeta-specific **primers**. Using the **Vbeta**/Cbeta **primers**, we observed limited **TCR** diversity only in recipients of a T-cell-depleted graft, whereas the **TCR** diversity of patients transplanted with an unmanipulated graft seemed to be indistinguishable from the one of a normal individual. However, with **Vbeta**/Jbeta-specific **primers**, increase of the resolution by approximately 10-fold also allowed the detection of imbalances in the **TCR** repertoire of recipients of an unmanipulated graft. This demonstrates that when high numbers of T cells are cotransfused with marrow, the **TCR** repertoire is more complete but still not as complete as in normal individuals, thereby emphasizing the important role of coinfused mature T cells in the restoration of the T-cell compartment after bone marrow transplantation.

=> s ky R?/au
L12 1 KY R?/AU

=> s kay R?/au
L13 2289 KAY R?/AU

=> s l13 and TCR
L14 32 L13 AND TCR

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15 18 DUP REM L14 (14 DUPLICATES REMOVED)

=> dis l15 1-18 ibib abs

L15 ANSWER 1 OF 18 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000429067 MEDLINE
DOCUMENT NUMBER: 20384795
TITLE: Antigen triggering selectively increases TCRBV gene transcription.
AUTHOR: Lennon G P; Sillibourne J E; Furrie E; Doherty M J; **Kay R A**
CORPORATE SOURCE: Department of Molecular and Cellular Pathology, University of Dundee, Ninewells Hospital and Medical School, Dundee, United Kingdom.
SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Aug 15) 165 (4) 2020-7. Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Abridged Index Medicus Journals
ENTRY MONTH: 200011
ENTRY WEEK: 20001103
AB When the **TCR** binds Ag it is phosphorylated, internalized, and degraded. We wished to examine whether this process was accompanied by a specific concomitant increase in **TCR** mRNA levels. To do this, PBMC and a T cell clone were cultured with a series of superantigens and an alloantigen. Only T cells specifically responding to an antigenic stimulus had increased levels of **TCR** beta-chain variable (TCRBV)-specific mRNA. This response was apparent after 48 h, peaked around 72 h, and was still elevated after 7 days. Increased gene transcription appeared to be driven solely by Ag as specific Ag depletion prevented culture supernatants transferring this effect. The level of TCRBV mRNA elevation was not influenced by the stimulating Ag, but appeared dependent on the gene encoding the stimulated **TCR**. Reporter gene assays, using cloned TCRBV gene promoters, confirmed both that **TCR** gene transcription rises after stimulation and that basal and stimulated levels of **TCR** transcription vary between different TCRBV genes. These data conclusively demonstrate that there is no direct relationship between TCRBV mRNA and T cell number, and that future repertoire studies must take both factors into account.

L15 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:226584 CAPLUS
DOCUMENT NUMBER: 130:236324
TITLE: Sequence analysis of DA and Sprague Dawley rat T-cell receptor .beta.-chain promoters. [Erratum to document cited in CA130:109050]
AUTHOR(S): Sillibourne, James E.; **Kay, Richard A.**
CORPORATE SOURCE: Dep. Molecular and Cellular Pathology, Ninewells Hospital and Medical School, Dundee, DD1 9SY, UK
SOURCE: Immunogenetics (1999), 49(3), 246 CODEN: IMNGBK; ISSN: 0093-7711
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Figs. 1 and 2 of this Sequence Register article were incorrect as

originally printed; the correct versions are given.

L15 ANSWER 3 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:154413 BIOSIS
DOCUMENT NUMBER: PREV200000154413
TITLE: The duodecamer motif is critical for both basal and stimulated TCRBV promoter function.
AUTHOR(S): Doherty, M. J. (1); Lennon, G. P. (1); Sillibourne, J. E. (1); Furrie, E. (1); **Kay, R. A. (1)**
CORPORATE SOURCE: (1) Dept. Molecular and Cellular Pathology, University of Dundee, Dundee, DD1 9SY UK
SOURCE: Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 123. Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy & Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy & Clinical Immunology . ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L15 ANSWER 4 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:139956 BIOSIS
DOCUMENT NUMBER: PREV200000139956
TITLE: The TCRBV13 **TCR** repertoire in anti-52 KDA Ro autoantibody-positive Sjogren's syndrome.
AUTHOR(S): Furrie, E. (1); Doherty, M. J. (1); Kershaw, A.; Crighton, A. J.; Morley, K.; **Kay, R. A. (1)**
CORPORATE SOURCE: (1) Dept. Molecular and Cellular Pathology, University of Dundee, Dundee, DD1 9SY UK
SOURCE: Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 33. Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy and Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy and Clinical Immunology . ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L15 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:795052 CAPLUS
DOCUMENT NUMBER: 130:37286
TITLE: Immunological method
INVENTOR(S): **Kay, Richard Andrew**
PATENT ASSIGNEE(S): University of Dundee, UK
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854223	A2	19981203	WO 1998-GB1382	19980527
WO 9854223	A3	19990304		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9876631	A1	19981230	AU 1998-76631	19980527
AU 728909	B2	20010118		
EP 1017724	A2	20000712	EP 1998-924427	19980527
R: CH, DE, FR, GB, IT, LI, NL, SE				
PRIORITY APPLN. INFO.:			GB 1997-10820	19970527
			WO 1998-GB1382	19980527

AB A method of identifying an antigen-responsive T cell within a population of T cells, the method comprising the steps of: (1) obtaining a sample contg. T cells which have responded to the antigen; (2) detg. individually for each of a plurality of specific T cell receptors, or individually for each of a plurality of subsets of T cell receptors, whether expression of a gene encoding a specific T cell receptor, or whether expression of genes encoding a subset of T cell receptors, has increased per specific T cell receptor-pos. T cell or per specific T cell receptor-pos. T cell subset compared to the expression of said gene or genes in a sample contg. T cells which have not responded to the antigen. The method is useful for identifying antigen-responsive T cells which are assocd. with a disease state such as rheumatoid arthritis.

L15 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:683257 CAPLUS
DOCUMENT NUMBER: 130:109050
TITLE: Sequence analysis of DA and Sprague Dawley rat T-cell receptor .beta.-chain promoters
AUTHOR(S): Sillibourne, James E.; **Kay, Richard A.**
CORPORATE SOURCE: Department of Molecular and Cellular Pathology, Ninewells Hospital and Medical School, Dundee, DD1 9SY, UK
SOURCE: Immunogenetics (1998), 48(5), 356-358
CODEN: IMNGBK; ISSN: 0093-7711
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The genomic sequences of 4 rat **TCR** .beta.-chain genes were analyzed in 1 inbred (DA) and 1 outbred (Sprague Dawley) rat strains. The sequences suggest that these promoters are capable of binding a comprehensive range of lineage-specific and non-lineage-specific factors, including putative binding sites for AP-1, AP-2, Sp1, GATA-binding factors, CREB, Ets-1, LEF-1, AML-1, and TCF-1. CAAT and TATA boxes were also identified in some of the promoters.
REFERENCE COUNT: 6
REFERENCE(S): (1) Halle, J; Mol Cell Biol 1997, V17, P4220 CAPLUS
(2) Kay, R; Eur J Immunol 1994, V24, P2863 CAPLUS
(3) Li, Y; J Exp Med 1991, V174, P1537 CAPLUS
(5) Rowen, L; Science 1996, V272, P1755 CAPLUS
(6) Smith, L; J Immunol 1991, V147, P375 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:125347 BIOSIS
DOCUMENT NUMBER: PREV199900125347
TITLE: Superantigens increase specific **TCR** gene transcription rates in unseparated human lymphocyte populations.
AUTHOR(S): Lennon, Greig; Sillibourne, James; **Kay, Richard**
CORPORATE SOURCE: Univ. Dep. Molecular Cellular Pathol., Ninewells Hosp. Med. Sch., Dundee DD1 9SY UK
SOURCE: Immunology, (Dec., 1998) Vol. 95, No. SUPPL. 1, pp. 28. Meeting Info.: 6th Annual Congress of the British Society for Immunology Harrogate, England, UK December 1-4, 1998 ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English

L15 ANSWER 8 OF 18 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 97414173 MEDLINE
DOCUMENT NUMBER: 97414173
TITLE: Long-term alloreactive T cell lines and clones express a limited T cell receptor repertoire.
AUTHOR: Tavakol Afshari J; Hutchinson I V; **Kay R A**
CORPORATE SOURCE: School of Biological Sciences, University of Manchester, UK.
SOURCE: TRANSPLANT IMMUNOLOGY, (1997 Jun) 5 (2) 122-8. Journal code: B32. ISSN: 0966-3274.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY WEEK: 19980104
AB Alloreactive T cells recognize either determinants of the intact donor MHC molecules displayed on the surface of transplanted-cells or peptide fragments of donor antigens associated with self-MHC molecules by means of their T cell receptors (**TCR**). To investigate the relationship between the **TCR** beta chain structure and allorecognition, we established and characterized four long-term T cell lines and seven T cell clones derived following a mixed lymphocyte reaction (MLR) between fully histoincompatible DA (RT1a) and LEW (RT1(1)) rat lymph node cells. These DA anti-LEW T cells were phenotypically CD4+, CD8-, alpha beta **TCR** + and produced interferon-gamma but not IL-4, consistent with being Th1 CD4+ T cells. As might be expected, these cells were not significantly cytotoxic and did not display suppressor activity. Analysis of the **TCR** beta chain gene structure revealed a very restricted repertoire in both long-term lines and clones. The TCRBV6S1 gene was present in 15/21 of the alloreactive T cell mRNA transcripts but only 1/12 of unstimulated DA splenic **TCR** mRNA transcripts ($p = 0.0018$). Similarly, the TCRBJ2S1 gene was also used frequently in the alloreactive transcripts (17/21) but in only 2/12 unstimulated splenic transcripts ($p = 0.0013$). Furthermore, all 15 of the alloreactive TCRBV6S1 transcripts had a distinctive four amino acid N region motif not present in any of the unstimulated **TCR** transcripts ($p = 0.0003$). These experiments reveal a distinct homogeneity amongst stable allogeneic T cells in culture. If these results reflect the situation in vivo, the possibility exists that specific immunotherapy may be successful in preventing allograft rejection.

L15 ANSWER 9 OF 18 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 96132972 MEDLINE
DOCUMENT NUMBER: 96132972
TITLE: Reduction of early B lymphocyte precursors in transgenic mice overexpressing the murine heat-stable antigen.
AUTHOR: Hough M R; Chappel M S; Sauvageau G; Takei F; **Kay R** ; Humphries R K
CORPORATE SOURCE: Terry Fox Laboratory, British Columbia Cancer Agency, Vancouver, Canada.
SOURCE: JOURNAL OF IMMUNOLOGY, (1996 Jan 15) 156 (2) 479-88. Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199604
AB To study the role of the murine heat-stable Ag (HSA) in lymphocyte maturation, we generated transgenic mice in which the HSA cDNA was under the transcriptional control of the **TCR** V beta promoter and Ig mu enhancer. The HSA transgene was expressed during all stages of B lymphocyte maturation. Expression was first detected in the earliest lymphoid-committed progenitors, which normally do not express HSA, and subsequently reached the highest levels in pro- and pre-B cells. In bone marrow, the number of IL-7-responsive clonogenic progenitors was < 4% of normal, whereas the frequency of earlier B lymphocyte-restricted precursors, detectable as Whitlock-Witte culture-initiating cells, was normal. Pro- and pre-B cells detected by flow cytometry were reduced by approximately 50% relative to controls. Mature splenic B cells were also reduced but to a lesser extent than in marrow, and their response to LPS stimulation was impaired. Reconstitution of SCID and BALB/c-nu/nu mice with HSA transgenic marrow indicated that the perturbations in B lymphopoiesis were not caused by a defective marrow microenvironment or by abnormal T cells. Our previous studies showed elevated HSA expression throughout thymocyte development, which resulted in a profound depletion of CD4+CD8+ double-positive and single-positive thymocytes. Together, these results indicate that HSA levels can determine the capacity of early T and B lymphoid progenitors to proliferate and survive. Therefore, HSA could serve as an important regulator during the early stages of B and T lymphopoiesis.

L15 ANSWER 10 OF 18 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 96303221 MEDLINE
DOCUMENT NUMBER: 96303221
TITLE: **TCR** gene polymorphisms and autoimmune disease.
AUTHOR: **Kay R A**
CORPORATE SOURCE: Department of Pathology, Ninewells Hospital & Medical School, Dundee, UK.
SOURCE: EUROPEAN JOURNAL OF IMMUNOGENETICS, (1996 Apr) 23 (2) 161-77. Ref: 129
Journal code: AZ6. ISSN: 0960-7420.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612

AB Autoimmunity may result from abnormal regulation within the immune system. As the T cell is the principal regulator of the immune system and its normal function depends on immune recognition or self/non-self discrimination, abnormalities of the idiotypic T-cell receptor (**TCR**) may be one cause of autoimmune disease. The **TCR** is a clonally distributed, cell-surface heterodimer which binds peptide antigen when complexed with HLA molecules. In order to recognize the variety of antigens it may possibly encounter, the **TCR**, by necessity, is a diverse structure. As with immunoglobulin, it is the variable domain of the **TCR** which interacts with antigen and exhibits the greatest amount of amino acid variability. The underlying genetic basis for this structural diversity is similar to that described for immunoglobulin, with **TCR** diversity relying on the somatic recombination, in a randomly imprecise manner, of smaller gene segments to form a functional gene. There are a large number of gene segments to choose from (particularly the TCRAV, TCRAJ and TCRBV gene segments) and some of these also exhibit allelic variation. Finally, polymorphisms in non-coding regions of **TCR** genes, leading to biased recombination or expression, are also beginning to be recognized. All these factors contribute to the polymorphic nature of the **TCR**, in terms of both structure and repertoire formation. It follows that inherited abnormalities in either coding or regulatory regions of **TCR** genes may predispose to aberrant T-cell function and autoimmune disease. This review will outline the genomic organization of the **TCR** genes, the genetic mechanisms responsible for the generation of diversity, and the results of investigations into the association between germline polymorphisms and autoimmune disease.

L15 ANSWER 11 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1995:384429 BIOSIS
DOCUMENT NUMBER: PREV199598398729
TITLE: Limited heterogeneity of **TCR** V-beta gene utilisation by alloreactive T cells.
AUTHOR(S): Tavakoli, J.; Hutchinson, I. V.; **Kay, R.**
CORPORATE SOURCE: Univ. Manchester, Med. Sch., Manchester M13 9PT UK
SOURCE: 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY.. (1995) pp. 646. The 9th International Congress of Immunology. Publisher: 9th International Congress of Immunology San Francisco, California, USA. Meeting Info.: Meeting Sponsored by the American Association of Immunologists and the International Union of Immunological Societies San Francisco, California, USA July 23-29, 1995
DOCUMENT TYPE: Conference
LANGUAGE: English

L15 ANSWER 12 OF 18 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 96023322 MEDLINE
DOCUMENT NUMBER: 96023322
TITLE: A subset of Sjogren's syndrome associates with the TCRBV13S2 locus but not the TCRBV2S1 locus.
AUTHOR: **Kay R A**; Hutchings C J; Ollier W E
CORPORATE SOURCE: Immunology Research Group, University of Manchester, United Kingdom..
SOURCE: HUMAN IMMUNOLOGY, (1995 Apr) 42 (4) 328-30. Journal code: G9W. ISSN: 0198-8859.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601

AB HGPSS associates with the TCRBV6S7 locus within the **TCR** beta-chain gene complex. However, V beta 6.7 T cells, encoded by this locus, have never been implicated in the salivary gland destruction that characterizes primary Sjogren's syndrome. Both V beta 13 and V beta 2 T cells have been implicated in glandular destruction. We therefore analyzed the association of HGPSS with both TCRBV2S1, the only TCRBV2 locus, and the TCRBV13S2 locus (the TCRBV13 family member which lies closest to TCRBV6S7). Our results show that the prevalence of TCRBV13S2*2 homozygotes is significantly increased in HGPSS and that there is a high degree of linkage disequilibrium between this locus and TCRBV6S7 not previously described across the **TCR** beta-chain gene complex. However, HGPSS does not associate with the TCRBV2S1 locus. These results suggest that it is the V beta 13.2 T cell which may be responsible for the autoimmune destruction that characterizes HGPSS and that the previous association of this condition with the TCRBV6S7 locus is primary due to the linkage disequilibrium that exists between it and TCRBV13S2.

L15 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:204308 CAPLUS
DOCUMENT NUMBER: 122:184945
TITLE: Genetic control of the human V.beta.13.2 T cell repertoire: importance of allelic variation outside the coding regions of the TCRBV13S2 gene
AUTHOR(S): **Kay, Richard A.**; Snowden, Neil; Hajeer, Ali H.; Boylston, Art W.; Ollier, William E. R.
CORPORATE SOURCE: Immunology Research Group, Univ. Manchester, Leeds, UK
SOURCE: Eur. J. Immunol. (1994), 24(11), 2863-7 CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In humans, the T cell repertoire is influenced by HLA, T cell receptor null alleles and antigen. Here, the authors describe a novel mechanism, independent of superantigen or T cell receptor structure which influences the T cell repertoire in a V.beta.-dependent manner. The authors have identified a biallelic locus, the TCRBV13S2 T cell receptor gene, where allelic differences predominate in the non-coding regions including transitions, transversions and frameshift deletions. The expressed protein is non-polymorphic at this locus. The TCRBV13S2 genotype profoundly influences the circulating level of V.beta.13.2 CD4 T cells but does not affect T cell receptor expression or function.

L15 ANSWER 14 OF 18 MEDLINE
ACCESSION NUMBER: 95135387 MEDLINE
DOCUMENT NUMBER: 95135387
TITLE: [Idiotypic T-lymphocyte receptor in animal and human autoimmune diseases]. Le recepteur idiotypique des lymphocytes T dans les maladies auto-immunes animales et humaines.
AUTHOR: **Kay R A**; Ollier W E

CORPORATE SOURCE: ACR Epidemiology Research Unit, Manchester, Grande Bretagne, UK..
SOURCE: REVUE DU RHUMATISME. EDITION FRANCAISE, (1994) 61 (7-8) 532-45. Ref: 147
Journal code: BQU.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505

AB Animal models have demonstrated that the T-cell repertoire is restricted when the response to defined autoantigens is studied. Anti-V beta specific monoclonal antibodies or specific V beta-derived peptides can be used to manipulate autoreactive T-cells to either prevent or treat established experimental disease in animals. In some animal models of arthritis, inherited differences in the **TCR** repertoire can protect against the development of experimental autoimmune disease. Human studies have generally given conflicting results with regard to the role of the **TCR** complexes as susceptibility loci for disease. This may be due to the heterogeneity present in the human population and/or in the diseases studied. In some diseases, where there is convincing evidence for putative autoantigens (multiple sclerosis) or distinct immunodysfunctional pathology (hypergammaglobulinaemic primary Sjogren's syndrome), restricted **TCR** repertoires and germline **TCR** susceptibility loci can be discerned. Recent evidence suggests that autoimmune disease may eventually be mapped to regulatory regions of the **TCR** V genes rather than the allelic differences in coding region structure. This may have implications for the future therapy of autoimmune rheumatic disease.

L15 ANSWER 15 OF 18 MEDLINE
ACCESSION NUMBER: 95135386 MEDLINE
DOCUMENT NUMBER: 95135386
TITLE: [T-lymphocyte receptor genes: genome organization and genetic mechanisms of repertoire diversity].
G`enes du recepteur des lymphocytes T: organisation genomique et mecanismes genetiques de la diversite du repertoire.
AUTHOR: **Kay R A**; Ollier W E
CORPORATE SOURCE: ACR Epidemiology Research Unit, Manchester, UK..
SOURCE: REVUE DU RHUMATISME. EDITION FRANCAISE, (1994) 61 (7-8) 521-31. Ref: 104
Journal code: BQU.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505

AB The T-cell receptor (**TCR**) is fundamental to the immune process in both health and disease. Reviewed here is the genetic organisation of the gene complexes which encode the **TCR** polypeptide chains alpha, beta, gamma, and delta. The **TCR** is by necessity a diverse structure and we consider the genetic mechanisms responsible for this. These include multiple variable gene segment isotypes, somatic recombination of gene segments, imprecisions in the recombination process and allelic variations in gene segments structure and regulation.

L15 ANSWER 16 OF 18 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94298865 EMBASE
DOCUMENT NUMBER: 1994298865
TITLE: Idiotypic T-cell receptor studies in animal and human autoimmune disease.
AUTHOR: **Kay R.A.**; Ollier W.E.R.
CORPORATE SOURCE: ACR Epidemiology Research Unit, Oxford Road,Manchester M13 9PT, United Kingdom
SOURCE: Revue du Rhumatisme (English Edition), (1994) 61/7-8 (470-482).
ISSN: 1169-8446 CODEN: RRHUEX
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LANGUAGE: English
SUMMARY LANGUAGE: English; French

AB Animal models have demonstrated that the T-cell repertoire is restricted when the response to defined autoantigens is studied. Anti-V.beta. specific monoclonal antibodies or specific V.beta.-derived peptides can be used to manipulate autoreactive T-cells to either prevent or treat established experimental disease in animals. In some animal models of arthritis, inherited differences in the **TCR** repertoire can protect against the development of experimental autoimmune disease. Human studies have generally given conflicting results with regard to the role of the **TCR** complexes as susceptibility loci for disease. This may be due to the heterogeneity present in the human population and/or in the diseases studied. In some diseases, where there is convincing evidence for putative autoantigens (multiple sclerosis) or distinct immunodysfunctional pathology (hypergammaglobulinaemic primary Sjogren's syndrome), restricted **TCR** repertoires and germline **TCR** susceptibility loci can be discerned. Recent evidence suggests that autoimmune disease may eventually be mapped to regulatory regions of the **TCR** V genes rather than the allelic differences in coding region structure. This may have implications for the future therapy of autoimmune rheumatic disease.

L15 ANSWER 17 OF 18 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94298864 EMBASE
DOCUMENT NUMBER: 1994298864
TITLE: The T-cell receptor genes: Genomic organisation and the genetic basis of repertoire diversity.
AUTHOR: **Kay R.A.**; Ollier W.E.R.
CORPORATE SOURCE: ACR Epidemiology Research Unit, Oxford Road,Manchester M13 9PT, United Kingdom
SOURCE: Revue du Rhumatisme (English Edition), (1994) 61/7-8 (459-469).
ISSN: 1169-8446 CODEN: RRHUEX
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
026 Immunology, Serology and Transplantation

031 Arthritis and Rheumatism
LANGUAGE: English
SUMMARY LANGUAGE: English; French
AB The T-cell receptor (**TCR**) is fundamental to the immune process in both health and disease. Reviewed here is the genetic organisation of the gene complexes which encode the **TCR** polypeptide chains .alpha., .beta., .gamma. and .delta.. The **TCR** is by necessity a diverse structure and we consider the genetic mechanisms responsible for this. These include multiple variable gene segment isotypes, somatic recombination of gene segments, imprecisions in the recombination process and allelic variations in gene segment structure and regulation.

L15 ANSWER 18 OF 18 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 91322881 MEDLINE
DOCUMENT NUMBER: 91322881
TITLE: An abnormal T cell repertoire in hypergammaglobulinaemic primary Sjogren's syndrome.
AUTHOR: **Kay R A**; Hay E M; Dyer P A; Dennett C; Green L M; Bernstein R M; Holt P J; Pumphrey R S; Boylston A W; Ollier W E
CORPORATE SOURCE: Regional Immunology Service, St Mary's Hospital, Manchester, UK..
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1991 Aug) 85 (2) 262-4.
Journal code: DD7. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199111
AB T cell antigen specificity is determined by the products of the genes which encode the variable regions of their receptors. Of the T cell receptor (**TCR**) variable region gene products examined, only V beta 6.7a **TCR**-positive lymphocytes were reduced in primary Sjogren's syndrome patients with IgG1 hypergammaglobulinaemia compared with an age-, sex- and HLA-matched control population. The levels of V beta 6.7a T cells were also significantly reduced when these patients were compared with an age- and sex-matched but HLA-unmatched control group and non-tissue typed normal people of both sexes. Since published studies show no such abnormality in rheumatoid arthritis, systemic lupus erythematosus or other autoimmune diseases, this abnormality may reflect a pathogenic process specific to primary Sjogren's syndrome.

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
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CA SUBSCRIBER PRICE	-4.70	-4.70

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=> s TCR and ((degenerate or generic) (5N) primer?)
L1 55 TCR AND ((DEGENERATE OR GENERIC) (5N) PRIMER?)

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2 17 DUP REM L1 (38 DUPLICATES REMOVED)

=> dis l2 1-17 ibibi abs kwic
'IBIBI' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

=> dis l2 1-17 ibib abs kwic

L2 ANSWER 1 OF 17 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001099135 MEDLINE
DOCUMENT NUMBER: 20565479
TITLE: T-cell antigen receptors in Atlantic cod (Gadus morhua l.): structure, organisation and expression of **TCR** alpha and beta genes.
AUTHOR: Wermenstam N E; Pilstrom L
CORPORATE SOURCE: Immunology Programme, Department of Cell and Molecular Biology, BMC, Uppsala University, Box 596, S-751 24, Uppsala, Sweden.
SOURCE: DEVELOPMENTAL AND COMPARATIVE IMMUNOLOGY, (2001 Mar) 25 (2) 117-35.
Journal code: E3M. ISSN: 0145-305X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ133844; GENBANK-AJ133845; GENBANK-AJ133846; GENBANK-AJ133847; GENBANK-AJ133848; GENBANK-AJ133849; GENBANK-AJ133850; GENBANK-AJ133851
ENTRY MONTH: 200102
AB By using short **degenerate primers** complementing conserved T-cell antigen receptor (**TCR**) variable and constant region segments for PCR, we were able to isolate putative TCRalpha and beta chain full length cDNAs in Atlantic cod. The Valpha and Vbeta domains have the canonical features of known teleost and mammalian **TCR** V domains, including conserved residues in the beginning of FR2 and at the end of FR3. The Jalpha and Jbeta region possess the conserved Phe-Gly-X-Gly motif found in nearly all **TCR** and immunoglobulin light chain J regions. Similar to other vertebrates, the Atlantic cod Calpha and Cbeta sequences exhibit distinct immunoglobulin, connecting peptide, transmembrane and cytoplasmic regions. The Atlantic cod Cbeta sequence lacks a cysteine in its connecting peptide region, but other motifs proposed to be important for dimerisation and cell surface expression are observed. Four different cod Cbeta sequences were identified, two of which share 3' untranslated regions different from one of the other two sequences, suggesting the existence of isotypic gene variants of Cbeta. Based on Southern blot analyses, the TCRalpha and beta gene loci appear to be arranged in translocon organisation (as opposed to multicluster) with multiple V gene segments, some (D) and J gene segments and a single or few C gene segments. Northern blot analyses show expression of the TCRalpha and beta chains in thymus, spleen and head kidney, expression of the TCRbeta chain was also detected in the ovary. Interestingly, no expression was detected in intestine even though the existence of T-cells in intestine has been proposed in other teleost species.
TI T-cell antigen receptors in Atlantic cod (Gadus morhua l.): structure, organisation and expression of **TCR** alpha and beta genes.
AB By using short **degenerate primers** complementing conserved T-cell antigen receptor (**TCR**) variable and constant region segments for PCR, we were able to isolate putative TCRalpha and beta chain full length cDNAs in Atlantic cod. The Valpha and Vbeta domains have the canonical features of known teleost and mammalian **TCR** V domains, including conserved residues in the beginning of FR2 and at the end of FR3. The Jalpha and Jbeta region possess the conserved Phe-Gly-X-Gly motif found in nearly all **TCR** and immunoglobulin light chain J regions. Similar to other vertebrates, the Atlantic cod Calpha and Cbeta sequences exhibit distinct immunoglobulin,. . .

L2 ANSWER 2 OF 17 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000171513 MEDLINE
DOCUMENT NUMBER: 20171513
TITLE: Description of an ectothermic **TCR** coreceptor, CD8 alpha, in rainbow trout.
AUTHOR: Hansen J D; Strassburger P
CORPORATE SOURCE: Basel Institute for Immunology, Basel, Switzerland.. hansen@bii.ch
SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Mar 15) 164 (6) 3132-9.
Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-AF178053; GENBANK-AF178054; GENBANK-AF178055
ENTRY MONTH: 200006
ENTRY WEEK: 20000601
AB We have cloned the first CD8 alpha gene from an ectothermic source using a **degenerate primer** for Ig superfamily V domains. Similar to homologues in higher vertebrates, the rainbow trout CD8 alpha gene encodes a 204-aa mature protein composed of two extracellular domains including an Ig superfamily V domain and hinge region. Differing from mammalian CD8 alpha V domains, lower vertebrate (trout and chicken) sequences do not contain the extra cysteine residue (C strand) involved in the abnormal intrachain disulfide bridging within the CD8 alpha V domain of mice and rats. The trout membrane proximal hinge region contains the two essential cysteine residues involved in CD8 dimerization (alpha alpha or alpha beta) and threonine, serine, and proline residues which may be involved in multiple O-linked glycosylation events. Although the transmembrane region is well conserved in all CD8 alpha sequences analyzed to date, the putative trout cytoplasmic region differs and, in fact, lacks the consensus p56lck motif common to other CD8 alpha sequences. We then determined that the trout CD8 alpha genomic structure is similar to that of humans (six exons) but differs from that of mice (five exons).

Additionally, Northern blotting and RT-PCR demonstrate that trout CD8 alpha is expressed at high levels within the thymus and at weaker levels in the spleen, kidney, intestine, and peripheral blood leukocytes. Finally, we show that trout CD8 alpha can be expressed on the surface of cells via transfection. Together, our results demonstrate that the basic structure and expression of CD8 alpha has been maintained for more than 400 million years of evolution.

TI Description of an ectothermic **TCR** coreceptor, CD8 alpha, in rainbow trout.

AB We have cloned the first CD8 alpha gene from an ectothermic source using a **degenerate primer** for Ig superfamily V domains. Similar to homologues in higher vertebrates, the rainbow trout CD8 alpha gene encodes a 204-aa. . .

L2 ANSWER 3 OF 17 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2000411646 MEDLINE
DOCUMENT NUMBER: 20394656
TITLE: Immunopurification of T-cells from sea bass Dicentrarchus labrax (L.).
AUTHOR: Scapigliati G; Romano N; Abelli L; Meloni S; Ficca A G; Buonocore F; Bird S; Secombes C J
CORPORATE SOURCE: Dipartimento di Scienze Ambientali, Universit`a della Tuscia, Viterbo, Italy.. scapigg@unitus.it
SOURCE: Fish Shellfish Immunol, (2000 May) 10 (4) 329-41. Journal code: DR8. ISSN: 1050-4648.
PUB. COUNTRY: ENGLAND: United Kingdom
LANGUAGE: Journal; Article; (JOURNAL ARTICLE) English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY WEEK: 20001101

AB The monoclonal antibody DLT15, specific for thymocytes and peripheral T-cells of the teleost fish Dicentrarchus labrax (sea bass), was used to purify immunoreactive cells from blood and gut-associated lymphoid tissue. The purification was performed by immuno-magnetic sorting of leucocyte fractions enriched by Percoll density gradient centrifugation, and the purity of the isolated cells was estimated by cytofluorimetric analysis. Following a single step, the percentage of DLT15-purified cells was 88 +/- 10% for gut-associated lymphoid tissue and 79 +/- 18% for blood leucocytes. DLT15-purified cells from gut-associated lymphoid tissue were employed for RNA extraction and cDNA synthesis. In RT-PCR experiments using as **primers degenerate** oligonucleotides corresponding to the peptide sequence MYWY and VYFCA of the trout **TcR** beta chain, a 203 bp product was amplified. When sequenced, the cDNA was found to show 60% nucleotide identity to the trout TcRV beta 3. By 3'-RACE the cDNA was elongated to obtain the **TcR** constant region, with high similarity to other fish **TcR** sequences. These results strongly suggest that cells recognised by DLT15 are putative T lymphocytes.

AB . . . leucocytes. DLT15-purified cells from gut-associated lymphoid tissue were employed for RNA extraction and cDNA synthesis. In RT-PCR experiments using as **primers degenerate** oligonucleotides corresponding to the peptide sequence MYWY and VYFCA of the trout **TcR** beta chain, a 203 bp product was amplified. When sequenced, the cDNA was found to show 60% nucleotide identity to the trout TcRV beta 3. By 3'-RACE the cDNA was elongated to obtain the **TcR** constant region, with high similarity to other fish **TcR** sequences. These results strongly suggest that cells recognised by DLT15 are putative T lymphocytes.

L2 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 4
ACCESSION NUMBER: 2000:853499 CAPLUS
TITLE: T-cell antigen receptors in Atlantic cod (Gadus morhua L.): structure, organisation and expression of **TCR** .alpha. and .beta. genes
AUTHOR(S): Wermenstam, N. E.; Pilstrom, L.
CORPORATE SOURCE: BMC, Department of Cell and Molecular Biology, Immunology Programme, Uppsala University, Uppsala, S-751 24, Swed.
SOURCE: Dev. Comp. Immunol. (2000), 25(2), 117-135 CODEN: DCIMDQ; ISSN: 0145-305X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB By using short **degenerate primers** complementing conserved T-cell antigen receptor (**TCR**) variable and const. region segments for PCR, we were able to isolate putative **TCR** .alpha. and .beta. chain full length cDNAs in Atlantic cod. The V.alpha. and V.beta. domains have the canonical features of known teleost and mammalian **TCR** V domains, including conserved residues in the beginning of FR2 and at the end of FR3. The J.alpha. and J.beta. region possess the conserved Phe-Gly-X-Gly motif found in nearly all **TCR** and Ig light chain J regions. Similar to other vertebrates, the Atlantic cod C.alpha. and C.beta. sequences exhibit distinct Ig, connecting peptide, transmembrane and cytoplasmic regions. The Atlantic cod C.beta. sequence lacks a cysteine in its connecting peptide region, but other motifs proposed to be important for dimerization and cell surface expression are obsd. Four different cod C.beta. sequences were identified, two of which share 3' untranslated regions different from one of the other two sequences, suggesting the existence of isotypic gene variants of C.beta.. Based on Southern blot analyses, the **TCR** .alpha. and .beta. gene loci appear to be arranged in translocon organization (as opposed to multicluster) with multiple V gene segments, some (D) and J gene segments and a single or few C gene segments. Northern blot analyses show expression of the **TCR**.alpha. and .beta. chains in thymus, spleen and head kidney, expression of the **TCR**.beta. chain was also detected in the ovary. Interestingly, no expression was detected in intestine even though the existence of T-cells in intestine has been proposed in other teleost species.

REFERENCE COUNT: 57
REFERENCE(S):
(2) Alcover, A; J Biol Chem 1990, V265, P4131 CAPLUS
(3) Arnaud, J; Int Immunol 1997, V9, P615 CAPLUS
(5) Backstrom, B; Science 1998, V281, P835 CAPLUS
(6) Bengten, E; Dev Comp Immunol 1994, V18, P109 CAPLUS
(7) Bengten, E; Eur J Immunol 1991, V21, P3027 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI T-cell antigen receptors in Atlantic cod (Gadus morhua L.): structure, organisation and expression of **TCR** .alpha. and .beta. genes

AB By using short **degenerate primers** complementing conserved T-cell antigen receptor (**TCR**) variable and const. region segments for PCR, we were able to isolate putative **TCR**

.alpha. and .beta. chain full length cDNAs [redacted]tlantic cod. The V.alpha. and V.beta. domains have the canonical features of known teleost and mammalian **TCR** V domains, including conserved residues in the beginning of FR2 and at the end of FR3. The J.alpha. and J.beta. region possess the conserved Phe-Gly-X-Gly motif found in nearly all **TCR** and Ig light chain J regions. Similar to other vertebrates, the Atlantic cod C.alpha. and C.beta. sequences exhibit distinct Ig, connecting peptide, transmembrane and cytoplasmic regions. The Atlantic cod C.beta. sequence lacks a cysteine in its connecting peptide region, but other motifs proposed to be important for dimerization and cell surface expression are obsd. Four different cod C.beta. sequences were identified, two of which share 3' untranslated regions different from one of the other two sequences, suggesting the existence of isotypic gene variants of C.beta.. Based on Southern blot analyses, the **TCR** .alpha. and .beta. gene loci appear to be arranged in translocon organization (as opposed to multicluster) with multiple V gene segments, some (D) and J gene segments and a single or few C gene segments. Northern blot analyses show expression of the **TCR**.alpha. and .beta. chains in thymus, spleen and head kidney, expression of the **TCR**.beta. chain was also detected in the ovary. Interestingly, no expression was detected in intestine even though the existence of T-cells in intestine has been proposed in other teleost species.

L2 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:151255 CAPLUS
DOCUMENT NUMBER: 128:214967
TITLE: RAFTK (related adhesion focal tyrosine kinase) molecules involved in regulation of cellular processes and the genes encoding them
INVENTOR(S): Avraham, Shalom; Avraham, Hava; Groopman, Jerome E.
PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, Inc., USA
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9807870	A1	19980226	WO 1997-US14093	19970812
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9741479	A1	19980306	AU 1997-41479	19970812
PRIORITY APPLN. INFO.:			US 1996-703623	19960823
			US 1997-816462	19970313
			WO 1997-US14093	19970812

AB Protein tyrosine kinases that play a role in a no. of intracellular signal transduction processes are identified and characterized and genes encoding them are cloned. The kinases are called related adhesion focal tyrosine kinase or RAFTK. Modulation of RAFTK activity may be of use in the treatment of disease. CDNAs were cloned from megakaryocytes by PCR using **degenerate primers** for protein tyrosine kinases. Human and mouse cDNAs for RAFTK are very similar, indicating strong evolutionary conservation with lower levels of identity and similarity with pp125FAK. The protein lacks transmembrane domains, myristylation sites, and SH2 and SH3 domains and interacts with protein kinase C and paxillins. Stimulation of PC-12 cells with stem cell factor changed the interaction of RAFTK with protein kinase C from via the .delta.-subunit to via the .alpha.-subunit.

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IT **TCR** (T cell receptors)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(RAFTK and signal transduction by; bprRAFTK (related adhesion focal tyrosine kinase) mols. involved in regulation of cellular processes and genes encoding them)

L2 ANSWER 6 OF 17 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 97390715 MEDLINE
DOCUMENT NUMBER: 97390715
TITLE: An amphibian CD3 homologue of the mammalian CD3 gamma and delta genes.
AUTHOR: Dzialo R C; Cooper M D
CORPORATE SOURCE: Department of Medicine, University of Alabama at Birmingham 35294-3300, USA.
CONTRACT NUMBER: AI30879 (NIAID)
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Jul) 27 (7) 1640-7.
Journal code: EN5. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-M59925; GENBANK-X01451; GENBANK-X52993; GENBANK-X53430; GENBANK-M12728; GENBANK-X52994; GENBANK-X04145; GENBANK-Y00635; GENBANK-U78290; GENBANK-Y12326
ENTRY MONTH: 199710
ENTRY WEEK: 19971005

AB T cell receptor (**TCR**) genes have been identified in representatives of both cartilaginous and bony vertebrates. The CD3 chains that serve as signal transducing elements of the **TCR** complex in mammals have been defined to a limited extent in birds. In these studies a CD3 homologue was identified in an amphibian representative, Xenopus laevis, using **degenerate** oligomer **primers** designed from conserved regions of avian and mammalian CD3 gamma/delta subunits. The reverse transcriptase polymerase chain reaction amplified product of Xenopus splenocyte RNA was then used to isolate full-length cDNA clones from a splenic library. When employed as probes, the cDNA clones hybridized with a 1-kb mRNA transcript in Xenopus T cells, but not in other cell types. Comparison of the deduced amino acid sequence indicated

a similar degree of homology with mammali[redacted]d avian CD3 gamma and delta chains. Genomic analysis indicated that the Xenopus CD3 molecule is encoded by five exons, a structure resembling the mammalian CD3 delta gene rather than the seven exon CD3 gamma gene. Southern blot analysis and sequencing of the 5' flanking region failed to yield evidence of a related Xenopus gene. This amphibian CD3 gene thus appears to represent an ancestral form of the mammalian CD3 gamma and delta genes.

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L2 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:733370 CAPLUS
DOCUMENT NUMBER: 128:44336
TITLE: Human T cell receptor alpha and beta chain cDNA amplification with a consensus primer
AUTHOR(S): Moonka, Dilip K.; Loh, Elwyn Y.
CORPORATE SOURCE: Department Medicine, Division Gastrointestinal Diseases, University Pennsylvania Medical Center Cancer Center, Philadelphia, PA, USA
SOURCE: Antigen T Cell Recept. (1997), 238-265. Editor(s): Oksenberg, Jorge R. Landes: Austin, Tex. CODEN: 65HEAM
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The detn. of the variable and joining sequences of T cell receptors in different human T cell populations is of interest in many biol. contexts. The use of reverse transcriptase to synthesize cDNA from mRNA followed by PCR has greatly facilitated this effort. However, the presence of variable regions presents and obvious obstacle to making specific primers for the 5' end. This work describes a **degenerate**, consensus **primer** that binds to a relatively conserved area of the human .alpha. and .beta. **TCR** variable region.

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ST human **TCR** cDNA RT PCR primer

IT Genes (animal)
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(**Tcr**; human T cell receptor alpha and beta chain cDNA amplification with a consensus primer)

IT **TCR** (T cell receptors)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha. and .beta. chains; human T cell receptor alpha and beta chain cDNA amplification with a consensus primer)

L2 ANSWER 8 OF 17 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 97205328 MEDLINE
DOCUMENT NUMBER: 97205328
TITLE: alpha, beta, gamma, and delta T cell antigen receptor genes arose early in vertebrate phylogeny.
AUTHOR: Rast J P; Anderson M K; Strong S J; Luer C; Litman R T; Litman G W
CORPORATE SOURCE: Department of Pediatrics, University of South Florida, All Children's Hospital, St. Petersburg 33701, USA.
CONTRACT NUMBER: R37 AI23338 (NIAID)
SOURCE: IMMUNITY, (1997 Jan) 6 (1) 1-11. Journal code: CCF. ISSN: 1074-7613.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U75747; GENBANK-U75748; GENBANK-U75749; GENBANK-U75750; GENBANK-U75751; GENBANK-U75752; GENBANK-U75753; GENBANK-U75754; GENBANK-U75755; GENBANK-U75756; GENBANK-U75757; GENBANK-U75758; GENBANK-U75759; GENBANK-U75760; GENBANK-U75761; GENBANK-U75762; GENBANK-U75763; GENBANK-U75764; GENBANK-U75765; GENBANK-U75766; GENBANK-U75767; GENBANK-U75768; GENBANK-U75769; GENBANK-U75770; GENBANK-U75771; GENBANK-U75772; GENBANK-U75773; GENBANK-U75774; GENBANK-U75775; GENBANK-U75776; +
ENTRY MONTH: 199706
ENTRY WEEK: 19970601

AB A series of products were amplified using a PCR strategy based on short minimally **degenerate primers** and R. eglanteria (clearnose skate) spleen cDNA as template. These products were used as probes to select corresponding cDNAs from a spleen cDNA library. The cDNA sequences exhibit significant identity with prototypic (alpha, beta, gamma, and delta T cell antigen receptor (**TCR**) genes. Characterization of cDNAs reveals extensive variable region diversity, putative diversity segments, and varying degrees of junctional diversification. This demonstrates expression of both alpha/beta and gamma/delta **TCR** genes at an early level of vertebrate phylogeny and indicates that the three major known classes of rearranging antigen receptors were present in the common ancestor of the present-day jawed vertebrates.

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L2 ANSWER 9 OF 17 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 96068761 MEDLINE
DOCUMENT NUMBER: 96068761
TITLE: Analysis of rearranged T-cell receptor beta-chain genes by polymerase chain reaction (PCR) DNA sequencing and automated high resolution PCR fragment analysis.
AUTHOR: Kneba M; Bolz I; Linke B; Hiddemann W
CORPORATE SOURCE: Department of Internal Medicine, Georg-August University, Goettingen, Germany.
SOURCE: BLOOD, (1995 Nov 15) 86 (10) 3930-7.
Journal code: A8G. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199602
AB Polymerase chain reaction (PCR)-directed amplification and sequencing of rearranged immune genes for identification of clone-specific markers are increasingly being used in acute lymphoblastic leukemia (ALL) and non-Hodgkin's lymphoma (NHL) patients instead of the time consuming and labor intensive Southern analysis. In previous reports, no single common V beta and J beta sequence had been identified that allowed reliable amplification of the majority of rearranged T-cell antigen receptor (**TCR**)-beta V-D-J junctions at the DNA level because of the relatively large number of possible **TCR**-beta variable (V beta) and joining (J beta) gene segments involved in the rearrangement processes. In the present study we designed highly **degenerate** PCR **primers** directed against conserved sequences of the J beta genes. IN combination with a previously published consensus V beta primer, these J beta primers specifically amplify **TCR**- beta V-N(D)N-J junctions from genomic DNA. Using this approach we studied DNA extracted from biopsy material of nine patients with T-cell lymphoproliferative disorders, one c-ALL patient, and five patients with nonmalignant diseases. T-cell lines Molt 3, Jurkat, and HM 2 served as monoclonal controls. Individual PCR products were sequenced after cloning. The nucleotide sequences of 96 randomly chosen recombinant vectors were determined. In the polyclonal controls all analyzed clones differed in their **TCR**-beta V-N(D)N-J junctions. In the T-cell lines, in all of the T-cell malignancies, and in the c-ALL, monoclonal PCR products could be identified by demonstration of clonally restricted V-N(D)N-J junctions. The PCR results were confirmed by automated fluorescence quantification and size determination of PCR products after separation in a high-resolution polyacrylamide gel. The procedure allows rapid and specific characterization of clonal **TCR**-beta rearrangements from genomic DNA and will significantly simplify current experimental approaches to identify and to quantitate malignant T cells during initial staging and follow-up of T-lineage NHL and ALL patients.
AB . . . beta and J beta sequence had been identified that allowed reliable amplification of the majority of rearranged T-cell antigen receptor (**TCR**)-beta V-D-J junctions at the DNA level because of the relatively large number of possible **TCR**-beta variable (V beta) and joining (J beta) gene segments involved in the rearrangement processes. In the present study we designed highly **degenerate** PCR **primers** directed against conserved sequences of the J beta genes. IN combination with a previously published consensus V beta primer, these J beta primers specifically amplify **TCR**- beta V-N(D)N-J junctions from genomic DNA. Using this approach we studied DNA extracted from biopsy material of nine patients with. . . nucleotide sequences of 96 randomly chosen recombinant vectors were determined. In the polyclonal controls all analyzed clones differed in their **TCR**-beta V-N(D)N-J junctions. In the T-cell lines, in all of the T-cell malignancies, and in the c-ALL, monoclonal PCR products could. . . determination of PCR products after separation in a high-resolution polyacrylamide gel. The procedure allows rapid and specific characterization of clonal **TCR**-beta rearrangements from genomic DNA and will significantly simplify current experimental approaches to identify and to quantitate malignant T cells during. . .

L2 ANSWER 10 OF 17 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 95369847 MEDLINE
DOCUMENT NUMBER: 95369847
TITLE: Identification and characterization of T-cell antigen receptor-related genes in phylogenetically diverse vertebrate species.
AUTHOR: Rast J P; Haire R N; Litman R T; Pross S; Litman G W
CORPORATE SOURCE: University of South Florida, All Children's Hospital, St. Petersburg 33701, USA.
CONTRACT NUMBER: RO1AI23338 (NIAID)
SOURCE: IMMUNOGENETICS, (1995) 42 (3) 204-12.
Journal code: GI4. ISSN: 0093-7711.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-U22666; GENBANK-U22667; GENBANK-U22668; GENBANK-U22669; GENBANK-U22670; GENBANK-U22671; GENBANK-U22672; GENBANK-U22673; GENBANK-U22674; GENBANK-U22675; GENBANK-U22676; GENBANK-U22677; GENBANK-U22678; GENBANK-U22679; GENBANK-U23067
ENTRY MONTH: 199511
AB Characterization of the structure, multiplicity, organization, and cell lineage-specific expression of T-cell receptor (**TCR**) genes of nonmammalian vertebrate species is central to the understanding of the evolutionary origins of rearranging genes of the vertebrate immune system. We recently described a polymerase chain reaction (PCR) strategy that relies on short sequence similarities shared by nearly all vertebrate **TCR** and immunoglobulin (Ig) variable (V) regions and have used this approach to isolate a **TCR** beta (TCRB) homolog from a cartilaginous fish. Using these short PCR products as probes in spleen cDNA and genomic libraries, we were able to isolate a variety of unique **TCR** and **TCR**-like genes. Here we report the identification and characterization of a chicken **TCR** gamma (TCRG) homolog, apparent Xenopus and pufferfish **TCR** alpha (TCRA) homologs, and two horned shark **TCR** delta (TCRD)-like genes. In addition, we have identified what could be a novel representative of the Ig gene superfamily in the pufferfish. This method of using short, minimally **degenerate** PCR **primers** should speed progress in the phylogenetic investigations of the **TCR** and related genes and lend important insights into both the origins and functions of these unique gene systems.
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lineage-specific expression of T-cell recep[redacted]TCR) genes of nonmammalian vertebrate species is central to the understanding of the evolutionary origins of rearranging genes of the vertebrate. . . . We recently described a polymerase chain reaction (PCR) strategy that relies on short sequence similarities shared by nearly all vertebrate **TCR** and immunoglobulin (Ig) variable (V) regions and have used this approach to isolate a **TCR** beta (TCRB) homolog from a cartilaginous fish. Using these short PCR products as probes in spleen cDNA and genomic libraries, we were able to isolate a variety of unique **TCR** and **TCR**-like genes. Here we report the identification and characterization of a chicken **TCR** gamma (TCRG) homolog, apparent Xenopus and pufferfish **TCR** alpha (TCRA) homologs, and two horned shark **TCR** delta (TCRD)-like genes. In addition, we have identified what could be a novel representative of the Ig gene superfamily in the pufferfish. This method of using short, minimally **degenerate** PCR **primers** should speed progress in the phylogenetic investigations of the **TCR** and related genes and lend important insights into both the origins and functions of these unique gene systems.

L2 ANSWER 11 OF 17 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 95369845 MEDLINE
DOCUMENT NUMBER: 95369845
TITLE: The recombination activation gene 1 (RAG1) of rainbow trout (Oncorhynchus mykiss): cloning, expression, and phylogenetic analysis.
AUTHOR: Hansen J D; Kaattari S L
CORPORATE SOURCE: Department of Microbiology, Oregon State University, Corvallis 97331-3804, USA..
CONTRACT NUMBER: ES05783 (NIEHS)
SOURCE: IMMUNOGENETICS, (1995) 42 (3) 188-95.
Journal code: GI4. ISSN: 0093-7711.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-U15663
ENTRY MONTH: 199511

AB The characterization of genes involved in the generation of the immune repertoire is an active area of research in lower vertebrate taxa. The recombination activating genes (RAG) have been shown to be essential for V (D) J recombination of T-cell antigen receptor (**TCR**) and immunoglobulin (Ig) genes, leading to the generation of the primary repertoire. As RAG1 is critical to the differentiation of pre-B and -T cells, its expression within an associated primary lymphoid organ can serve as a developmental marker. To examine the ontogeny of lymphocytes in Oncorhynchus mykiss, we cloned RAG1 from trout and examined its tissue- and lymphocyte-specific expression. The polymerase chain reaction, coupled with **degenerate** oligonucleotide **primers**, was used to amplify a homologous probe [(633 base pairs) (bp)] from rainbow trout genomic DNA, which in turn was used to isolate a lambda genomic clone. Sequence analysis of this genomic clone confirmed the RAG1 nature of this gene (3888 bp) and revealed an internal intron of 666 bp. When compared with other previously reported RAG1 sequences, the predicted amino acid translation (1073 aa) displayed a minimum of 78% similarity for the complete sequence and 89% similarity in the conserved region (aa 417-1042). Using northern blot analysis, we found the expression of RAG1 to be limited to surface Ig-n lymphocytes within the thymus. This data forms the basis for a proposal that the thymus of teleost species plays an essential developmental role in lymphopoiesis and thus can be regarded as a primary lymphoid organ.

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L2 ANSWER 12 OF 17 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 95252184 MEDLINE
DOCUMENT NUMBER: 95252184
TITLE: Cloning the rat homolog of the CD28/CTLA-4-ligand B7-1: structural and functional analysis.
AUTHOR: Judge T A; Liu M; Christensen P J; Fak J J; Turka L A
CORPORATE SOURCE: Department of Internal Medicine, University of Michigan Medical School, Ann Arbor 48109, USA..
CONTRACT NUMBER: MO1RR00042 (NCRR)
IF32CA62575-01 (NCI)
CA61225 (NCI)
SOURCE: INTERNATIONAL IMMUNOLOGY, (1995 Feb) 7 (2) 171-8.
Journal code: AY5. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U05593
ENTRY MONTH: 199508

AB T cell activation involves the delivery of two independent signals to the naive T cell. The first signal occurs with engagement of the **TCR** . One of the best characterized second signals is ligation of CD28 on the surface of T cells by B7 molecules (B7-1, B7-2) present on the surface of activated antigen presenting cells (APCs). Recent studies have demonstrated that injection of a human fusion protein, CTLA-4-Ig, which in humans binds to both B7-1 and B7-2, prevents cardiac allograft rejection in a rat transplantation model when given 48 h after engraftment. In order to better characterize the role of B7-1 (which is maximally expressed 48 h after activation of APCs) in this model, as well as in models of tumor-induced immune responses, we have cloned the rat homolog of B7-1, and now report on its structure and function. A 1030 bp cDNA containing the entire coding sequence of the rat B7-1 was cloned with a polymerase chain reaction strategy utilizing **degenerate primers** derived from published murine and human B7-1 sequences. The rat B7-1 coding sequence is 67 and 81% homologous to human and murine B7-1 cDNAs, and the predicted peptide sequence is likewise 57 and 66% identical to the peptide sequences of human and murine B7-1 respectively. The greatest area of identity occurs in the extracellular portion of the molecule, particularly the Ig-C like domain.(ABSTRACT TRUNCATED AT 250 WORDS)

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the best characterized second signals i[redacted]tion of CD28 on the surface of T cells by B7 molecules. . . . bp cDNA containing the entire coding sequence of the rat B7-1 was cloned with a polymerase chain reaction strategy utilizing **degenerate primers** derived from published murine and human B7-1 sequences. The rat B7-1 coding sequence is 67 and 81% homologous to human. . . .

L2 ANSWER 13 OF 17 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 95023888 MEDLINE
DOCUMENT NUMBER: 95023888
TITLE: T-cell receptor gene homologs are present in the most primitive jawed vertebrates.
AUTHOR: Rast J P; Litman G W
CORPORATE SOURCE: Department of Pediatrics, University of South Florida, All Children's Hospital, St. Petersburg 33701..
CONTRACT NUMBER: AI-23338 (NIAID)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Sep 27) 91 (20) 9248-52. Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Cancer Journals; Priority Journals
OTHER SOURCE: GENBANK-U07622; GENBANK-U07623; GENBANK-U07624; GENBANK-U09531; GENBANK-U09532; GENBANK-U09533; GENBANK-U09534
ENTRY MONTH: 199501
AB The phylogenetic origins of T-cell immunity and T-cell antigen receptor (**TCR**) genes have not been established. A PCR approach using short, minimally **degenerate** oligodeoxynucleotide **primers** complementing conserved variable region segments amplifies **TCR** -like products from the genomic DNA of Heterodontus francisci (horned shark), a representative phylogenetically primitive cartilaginous fish. One of these products has been used as a probe to screen a Heterodontus spleen cDNA library and a clone was identified that is most related at the nucleotide sequence and predicted peptide levels to higher vertebrate **TCR** beta-chain genes. Genomic analyses of the **TCR** homologs indicate that recombining variable and joining region segments as well as constant region exons are encoded by extensive gene families, organized in the multicluster form, characteristic of both the immunoglobulin heavy- and light-chain gene loci in the cartilaginous fishes. Greater numbers of homologous products were identified when a probe complementing the putative constant region of the **TCR** homolog was used to screen the same cDNA library. A high degree of intergenic variation is associated with the putative variable region segments of these isolates. Direct evidence is presented for **TCR** -like genes, which presumably are associated with T-cell function, at the earliest stages in the phylogenetic emergence of jawed vertebrates.
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L2 ANSWER 14 OF 17 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 94179857 MEDLINE
DOCUMENT NUMBER: 94179857
TITLE: A consensus primer to amplify both alpha and beta chains of the human T cell receptor.
AUTHOR: Moonka D; Loh E Y
CORPORATE SOURCE: Department of Medicine, University of Pennsylvania Medical Center, Philadelphia..
CONTRACT NUMBER: AI33214 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1994 Feb 28) 169 (1) 41-51. Journal code: IFE. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199406
AB The use of reverse transcriptase in conjunction with the polymerase chain reaction (RT-PCR) has proven invaluable in the analysis of the T cell receptor (**TCR**) repertoire of different populations of T cells. However, the presence of a variable region in the T cell receptor has hindered the design of primers for the 5' end of the **TCR** cDNA. We describe the design and use of a **degenerate** consensus **primer** that allows amplification of both the alpha and beta chains of the human **TCR**. We have used this primer in the analysis of the **TCR** distribution of T cell clones, peripheral blood lymphocytes and lymphocytes residing in tissue. In addition, the primer has allowed the identification of an alternative splice site in the beta chain constant region which cannot translate into a functional constant region. We have found the primer to be easy to use, sensitive and specific.
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L2 ANSWER 15 OF 17 MEDLINE DUPLICATE 13

ACCESSION NUMBER: 94014793 MEDLINE
DOCUMENT NUMBER: 94014793
TITLE: Ex vivo clonotype primer-directed gene amplification to identify malignant T cell repertoires.
AUTHOR: Beers T; Du T L; Rickert M; Overturf P; Choi Y; Greenberg S J
CORPORATE SOURCE: Department of Neurology, Roswell Park Cancer Institute, Buffalo, NY 14263.
SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (1993 Oct) 54 (4) 343-50. Journal code: IWY. ISSN: 0741-5400.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199401

AB A novel strategy that utilizes input genomic DNA and overcomes limitations encountered with traditional RNA reverse transcription-polymerase chain reaction (PCR) amplification methodology is described to screen for T cell receptor (**TCR**) repertoires. The methodology has been developed to identify individual T cell clonotypes with regard to their unique receptor beta chain variable/diversity/joining (VDJ) region gene rearrangement. The technique avoids preselection for a given antigen specificity and is therefore independent of artificial bias introduced by in vitro cell population expansion. This technique was used to detect and identify genetically of malignant clones from heterogeneous mononuclear cell populations from an array of hemato-oncological disorders, including mycosis fungoides/Sezary Syndrome, adult T cell leukemia, and large granular lymphoproliferative disease. An initial primary PCR, directed by a **TCR**-J beta **generic primer** and a complement of family-specific **TCR**-V beta primers, defines predominant T cell receptor variable gene usage. Use of a **TCR**-J beta **generic primer** supplants the use of a constant region primer anchor and thus eliminates the need to target mRNA. The process of variable gene screening also expedites gene sequencing. By sequencing through the VDJ juxtaposed region, i.e., the third complementarity determinant region, clonotype-specific primers are developed and used in a secondary clonotype primer-directed PCR (CPD-PCR) to detect, with extreme sensitivity and specificity, unique T cell clonal repertoires. Analysis of the products of the CPD-PCR permits the detection of a single malignant cell among one million polyclonal cells and supercedes the constraints of prior studies that provide a limited evaluation of family variable gene repertoire usage. This strategy may be applied in the detection of minimal residual disease, in surveillance after induction of disease-free states, and in analyzing the effectiveness of purging autologous bone marrow of malignant clones.

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L2 ANSWER 16 OF 17 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 91184261 MEDLINE
DOCUMENT NUMBER: 91184261
TITLE: Conserved nucleotide sequences at the 5' end of T cell receptor variable genes facilitate polymerase chain reaction amplification.
AUTHOR: Broeren C P; Verjans G M; Van Eden W; Kusters J G; Lenstra J A; Logtenberg T
CORPORATE SOURCE: Institute of Infectious Diseases and Immunology, School of Veterinary Medicine, University of Utrecht, The Netherlands..
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1991 Mar) 21 (3) 569-75. Journal code: EN5. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199107

AB Alignment of all available nucleotide sequences of mouse and rat alpha/beta T cell receptor (**TcR**) variable (V) regions revealed the presence of relatively conserved sequences at the 5' end of the V gene segments. Based on these conserved sequences, **degenerate primers** were developed for use in the polymerase chain reaction (PCR). The **degenerate primers** developed on the basis of the conserved sequences at the 5' end of rat and mouse V gene segments are expected to enable the amplification of all mouse and rat **TcR** alpha/beta chain V regions. To test their applicability, the primers were used for the amplification of the V region of the **TcR** alpha/beta expressed by rat T cell lines. After amplification, the **TcR** V regions expressed were cloned and sequenced. The Z1a T cell line was shown to use the same **TcR** V gene segments (V alpha 2 and V beta 8.2), as most other experimental allergic encephalomyelitis associated T cell lines, but had different D and J segments. In spite of these differences at the nucleotide level, a remarkable conservation of the amino acid sequence at the V beta D beta J beta junction was found. Alignment of a large number of human V alpha and V beta gene segments revealed the presence of similarly conserved sequences. **Degenerate primers** based on these conserved sequences enabled the amplification of **TcR** V regions of human T cell lines.

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L2 ANSWER 17 OF 17 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 90293689 MEDLINE
DOCUMENT NUMBER: 90293689
TITLE: The presumptive CDR3 regions of both T cell receptor alpha and beta chains determine T cell specificity for myoglobin peptides.
AUTHOR: Danska J S; Livingstone A M; Paragas V; Ishihara T; Fathman C G
CORPORATE SOURCE: Department of Medicine, Stanford University School of Medicine, California 94305..
CONTRACT NUMBER: AI-19512 (NIAID)
AI-27989 (NIAID)
DK-39959 (NIDDK)
+
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1990 Jul 1) 172 (1) 27-33.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199010

AB The T cell receptor alpha/beta (**TCR**-alpha/beta) is encoded by variable (V), diversity (D), joining (J), and constant (C) segments assembled by recombination during thymocyte maturation to produce a heterodimer that imparts antigenic specificity to the T cell. Unlike immunoglobulins (Igs), which bind free antigen, the ligands of **TCR** -alpha/beta are cell surface complexes of intracellularly degraded antigens (i.e., peptides) bound to and presented by polymorphic products of the major histocompatibility complex (MHC). Therefore, antigen recognition by T cells is defined as MHC restricted. A model has been formulated based upon the similarity between **TCR**-alpha/beta V region and Ig Fab amino acid sequences, and the crystal structure of the MHC class I and Ig molecules. This model predicts that the complementarity determining regions (CDR) 1 and 2, composed of **TCR** V alpha and V beta segments, primarily contact residues of the MHC alpha helices, whereas V/J alpha and V/D/J beta junctional regions (the CDR3 equivalent) contact the peptide in the MHC binding groove. Because polymorphism in MHC proteins is limited relative to the enormous diversity of antigenic peptides, the **TCR** may have evolved to position the highly diverse junctional residues (CDR3), where they have maximal contact with antigen bound in the MHC peptide groove. Here, we demonstrate a definitive association between CDR3 sequences in both **TCR** alpha and beta chains, and differences in recognition of antigen fine specificity using a panel of I-Ed-restricted, myoglobin-reactive T cell clones. Acquisition of these data relied in part upon a modification of the polymerase chain reaction that uses a **degenerate**, consensus **primer** to amplify **TCR** alpha chains without foreknowledge of the V alpha segments they utilize.

AB The T cell receptor alpha/beta (**TCR**-alpha/beta) is encoded by variable (V), diversity (D), joining (J), and constant (C) segments assembled by recombination during thymocyte maturation to. . . . a heterodimer that imparts antigenic specificity to the T cell. Unlike immunoglobulins (Igs), which bind free antigen, the ligands of **TCR** -alpha/beta are cell surface complexes of intracellularly degraded antigens (i.e., peptides) bound to and presented by polymorphic products of the major. . . . antigen recognition by T cells is defined as MHC restricted. A model has been formulated based upon the similarity between **TCR**-alpha/beta V region and Ig Fab amino acid sequences, and the crystal structure of the MHC class I and Ig molecules. This model predicts that the complementarity determining regions (CDR) 1 and 2, composed of **TCR** V alpha and V beta segments, primarily contact residues of the MHC alpha helices, whereas V/J alpha and V/D/J beta. . . . the MHC binding groove. Because polymorphism in MHC proteins is limited relative to the enormous diversity of antigenic peptides, the **TCR** may have evolved to position the highly diverse junctional residues (CDR3), where they have maximal contact with antigen bound in the MHC peptide groove. Here, we demonstrate a definitive association between CDR3 sequences in both **TCR** alpha and beta chains, and differences in recognition of antigen fine specificity using a panel of I-Ed-restricted, myoglobin-reactive T cell clones. Acquisition of these data relied in part upon a modification of the polymerase chain reaction that uses a **degenerate**, consensus **primer** to amplify **TCR** alpha chains without foreknowledge of the V alpha segments they utilize.

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